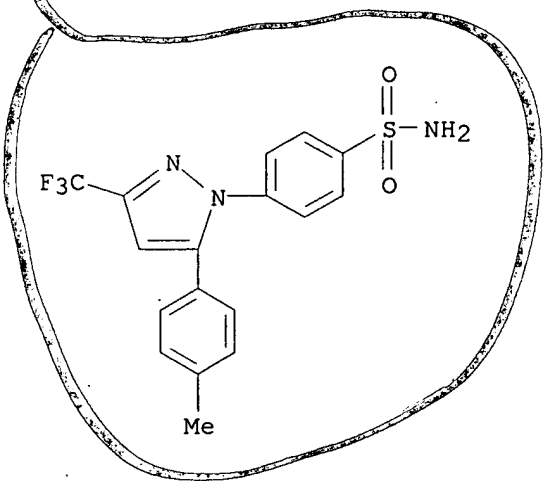
Structures

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 169590-42-5 REGISTRY
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
CN Celebrex
CN Celecoxib
CN Celocoxib
CN SC 58635
CN YM 177
FS 3D CONCORD
DR 184007-95-2, 194044-54-7
MF C17 H14 F3 N3 O2 S
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

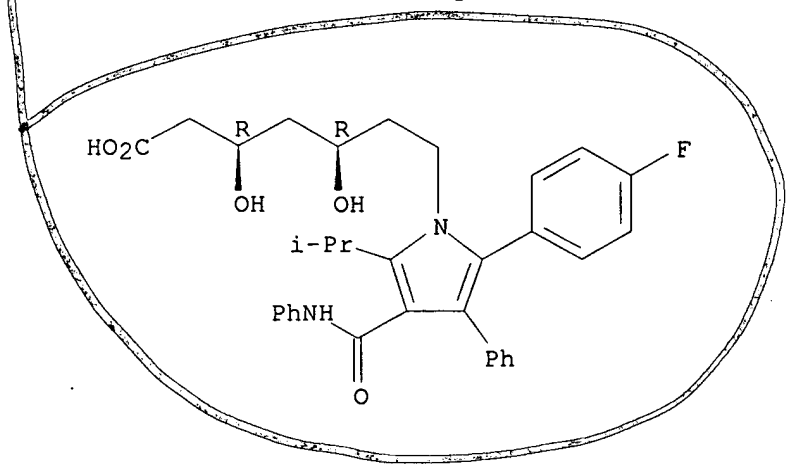


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

758 REFERENCES IN FILE CA (1907 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
778 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 134523-00-5 REGISTRY
CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-.beta.,.delta.-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, (.beta.R,.delta.R)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-.beta.,.delta.-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, [R-(R*,R*)]-
OTHER NAMES:
CN (.beta.R,.delta.R)-2-(p-Fluorophenyl)-.beta.,.delta.-dihydroxy-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)pyrrole-1-heptanoic acid
CN Atorvastatin
CN Cardyl
FS STEREOSEARCH
MF C33 H35 F N2 O5
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

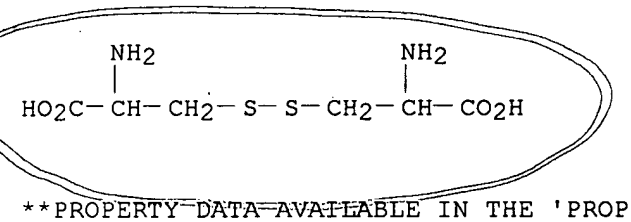
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1016 REFERENCES IN FILE CA (1907 TO DATE)
30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1029 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 923-32-0 REGISTRY
CN **Cystine (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cystine, DL- (8CI)
OTHER NAMES:
CN DL-Cystine
CN NSC 203781
FS 3D CONCORD
MF C6 H12 N2 O4 S2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PROMT, TOXCENTER, TULSA, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



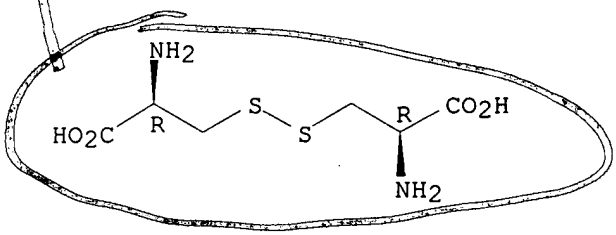
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

242 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
242 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 56-89-3 REGISTRY
CN L-Cystine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cystine, L- (8CI)
OTHER NAMES:
CN (-)-Cystine
CN .beta.,.beta.'-Diamino-.beta.,.beta.'-dicarboxydiethyl disulfide
CN .beta.,.beta.'-Dithiodialanine
CN 3,3'-Dithiobis(2-aminopropanoic acid)
CN Bis(.beta.-amino-.beta.-carboxyethyl) disulfide
CN **Cystine**
CN Cystine acid
CN Dicysteine
CN L-(-)-Cystine
CN L-Alanine, 3,3'-dithiobis-
CN L-Cysteine disulfide
CN L-Cystin
CN l-Cystine
CN NSC 13203
CN Oxidized L-cysteine
CN Propanoic acid, 3,3'-dithiobis[2-amino-, [R-(R*,R*)]-
CN [R-(R*,R*)]-3,3'-Dithiobis[2-aminopropanoic acid]
AR 24645-67-8

FS STEREOSEARCH
DR 24645-67-8
MF C6 H12 N2 O4 S2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



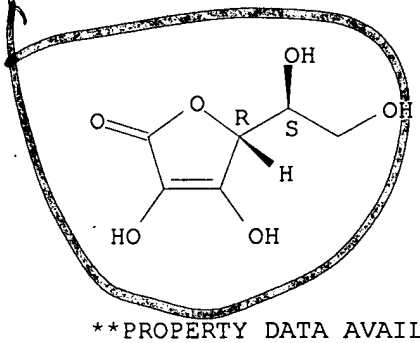
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12301 REFERENCES IN FILE CA (1907 TO DATE)
215 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
12306 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 50-81-7 REGISTRY
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-Ascorbic acid
CN 3-keto-L-Gulofuranolactone
CN 3-Oxo-L-gulofuranolactone
CN Adenex
CN Allercorb
CN Antiscorbic vitamin
CN Antiscorbutic vitamin
CN Ascoltin
CN Ascorbajen
CN Ascorbic acid
CN Ascorbicap
CN Ascorbutina
CN Ascorin
CN Ascorteal
CN Ascorvit
CN C-Quin
CN C-Vimin
CN Cantan
CN Cantaxin
CN Catavin C
CN Ce-Mi-Lin
CN Ce-Vi-Sol
CN Cebicure
CN Cebion
CN Cebion, .gamma.-lactone
CN Cebione
CN Cecon
CN Cegiolan
CN Ceglion
CN Ceklin
CN Celaskon
CN Celin
CN Cell C
CN Cemagyl
CN Cenetone
CN Cereon
CN Cergona
CN Cescorbat
CN Cetamid
CN Cetane
CN Cetane-Caps TC
CN Cetebe
CN Cetemican
CN Cevalin
CN Cevatine
CN Cevex
CN Cevimin
CN Cevital
CN Cevitamic acid
CN Cevitamin
CN Vitamin C
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for

DISPLAY
FS STEREOSEARCH
DR 623158-95-2, 56533-05-2, 57304-74-2, 57606-40-3, 56172-55-5, 129940-97-2, 14536-17-5, 50976-75-5, 154170-90-8, 89924-69-6, 30208-61-8, 259133-78-3
MF C6 H8 O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

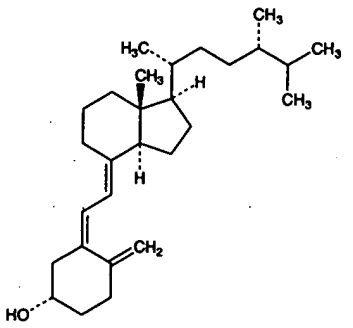
68771 REFERENCES IN FILE CA (1907 TO DATE)
1332 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
68884 REFERENCES IN FILE CAPLUS (1907 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 1406-18-4 REGISTRY
CN Vitamin E **(9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Aquasol E
CN Covitol F 1300
CN E-Mix 40
CN E-Mix 70L
CN Erevit forte
CN Evion
CN Fujimix E 20N
CN Hydrovit E forte
CN Irganox E 217
CN Irganox E 218
CN Juvela E
CN Juvela Food 500
CN MDE 6000
CN Palmvitee
CN Rocavit E
CN Rontex 201
DR 11105-14-9
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
17543 REFERENCES IN FILE CA (1907 TO DATE)
253 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17585 REFERENCES IN FILE CAPLUS (1907 TO DATE)

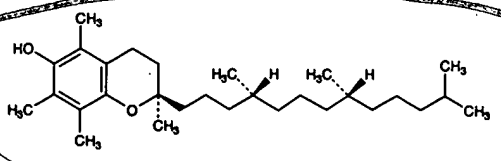
Merck Index

11.63%, O 4.01%. Prepd from 22:23-dihydroergosterol by irradiation with light of the magnesium arc: Windaus, Trautmann, *Z. Physiol. Chem.* **247**, 185 (1937). Synthesis: P. J. Kocienski *et al., J. Chem. Soc., Perkin Trans. I* **1979**, 1290.



Platelets from dil acetone, mp 96-98°. Originally given as mp 107-108°, *see* Windaus, Guntzel, *Ann.* **538**, 122 (1939). $[\alpha]_D^{18}$ +89.3° (c = 0.47 in acetone). uv max: 265 nm. Not precipitated by digitonin. Practically insol in water. Sol in the usual organic solvents except petr ether; slightly sol in vegetable oils.

10159. Vitamin E. ***[2R-[2R*(4R*,8R*)]-3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol; 2,5,7,8-tetramethyl-2-(4',8',12'-trimethyltridecyl)-6-chromanol;*** α-tocopherol; (+)-α-tocopherol; 5,7,8-trimethyltocol; antisterility vitamin. $C_{29}H_{50}O_2$; mol wt 430.71. C 80.87%, H 11.70%, O 7.43%. Found largely in plant materials. Present in highest concns (0.1-0.3%) in wheat germ, corn, sunflower seed, rapeseed, soybean oils, alfalfa and lettuce. Natural α-tocopherol is usually found with β- and γ-tocopherols, *q.q.v.* Isoln from wheat germ: Evans *et al., J. Biol. Chem.* **113**, 319 (1936). Structure: Fernholz, *J. Am. Chem. Soc.* **59**, 1154 (1937); **60**, 700 (1938). Synthesis: Karrer *et al., Helv. Chim. Acta* **21**, 520, 820 (1938); Bergel *et al., J. Chem. Soc.* **1938**, 1382; Smith *et al., Science* **88**, 37 (1938); Smith, Sprung, *J. Am. Chem. Soc.* **65**, 1276 (1943). Recent syntheses: N. Cohen *et al., Helv. Chim. Acta* **61**, 837 (1978); *eidem, J. Am. Chem. Soc.* **101**, 6710 (1979); R. Barner, M. Schmid, *Helv. Chim. Acta* **62**, 2384 (1979). Abs config of natural α-tocopherol: Mayer *et al., ibid.* **46**, 963 (1963). Stereoselective synthesis of the side chain: C. H. Heathcock, E. T. Jarvi, *Tetrahedron Letters* **23**, 2825 (1982). Review of industrial processes: Rubel, *Vitamin E Manufacture* (Noyes Dev. Corp., Park Ridge, N.J., 1969). *Reviews: The Vitamins* **Vol. 5**, W. H. Sebrell, R. S. Harris, Eds. (Academic Press, New York, 1972) pp 165-317; J. M. Bieri, P. M. Farrell, *Vitam. Horm. (New York)* **34**, 31-75 (1976). Book: *Ann. N.Y. Acad. Sci.* **393**, entitled "Vitamin E: Biochemical, Hematological and Clinical Aspects", B. Lubin, L. J. Machlin, Eds. (1982) 506 pp. Review of medical uses: J. G. Bieri *et al., N. Engl. J. Med.* **308**, 1063-1071 (1983).



$[\alpha]_{546}^{25}$ +3.0° (benzene); $[\alpha]_{5461}^{25}$ +0.32° (alc).

Succinate, *Vitamin E acid succinate.* Prepn: Demole *et al., Helv. Chim. Acta* **22**, 65 (1939); McArthur, Watson, *Can. Chem. Process Inds.* **23**, 350 (1939); Baxter *et al., J. Am. Chem. Soc.* **65**, 918 (1943). Needles from petr ether, mp 76-77°. uv max (ethanol): 286 nm ($E_{1cm}^{1\%}$ 38.5). Practically insol in water.

Nicotinate, $C_{35}H_{53}NO_3$, *Hijuven, Juvela Nicotinate, Renascin.*

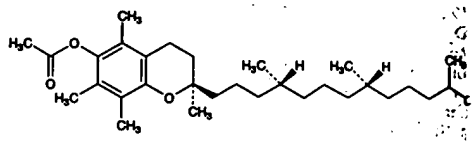
dl-Form, slightly viscous, pale yellow oil. Natural α-tocopherol has been crystallized, mp 2.5°-3.5°. d_4^{25} 0.950; $bp_{0.1}$ 200-220°; n_D^{25} 1.5045. uv max: 294 nm (E_{1c} Practically insol in water. Freely sol in oils, fats, ac alcohol, chloroform, ether, other fat solvents. Stable t and alkalies in the absence of oxygen. Not affected by up to 100°. Slowly oxidized by atm oxygen, rapid ferric and silver salts. Gradually darkens on expos light.

USE: As an antioxidant in vegetable oils and shorte

THERAP CAT: Treatment of vitamin E deficiency.

THERAP CAT (VET): Nutritional factor. Interrelatic with selenium. (Prevents muscle degeneration, also en alomalaria and exudative diathesis.) Has been used t mote fertility.

10160. Vitamin E Acetate. ***[2R*(4R*,8R*)]-3,4-dro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-, zopyran-6-ol acetate; 2,5,7,8-tetramethyl-2-(4,8,12-trim tridecyl)-6-chromanol acetate;*** α-tocopherol acetate; copheryl acetate; $C_{31}H_{52}O_3$; mol wt 472.75. C 78.76 11.09%, O 10.15%. Prepn from *dl*-α-tocopherol and anhydride: Surmatis, Weber, U.S. pat. 2,723,278 (19 Hoffmann-La Roche). Prepn of *d*- and *l*-forms: Rob Nelan, *J. Am. Chem. Soc.* **84**, 3196 (1962). Stereosel synthesis: K.-K. Chan *et al., J. Org. Chem.* **43**, 3435 (1 Total synthesis of all eight stereoisomers: N. Cohen *Helv. Chim. Acta* **64**, 1158 (1981). Comprehensive de tion: B. C. Rudy, B. Z. Senkowski, *Anal. Profiles Subs.* **3**, 111-126 (1974).



dl-Form, *Detulin, Ephynal, Eprolin, Epsilan-M, Ex E-Vimin, Evion, Juvela, OptoVit-E, Toco 500, Vitagutt,* yellow, viscous liquid. mp −27.5°. $d_4^{21.3}$ 0.9533. $bp_{0.1}$ $bp_{0.025}$ 194°; $bp_{0.3}$ 224°. n_D^{20} 1.4950-1.4972. uv max (c hexane): 285.5 nm. Practically insol in water. Freely s acetone, chloroform, ether. Less readily sol in alc. U the free vitamins, the acetate is practically unaffected b oxidizing influence of air, light, and ultraviolet light.

d-Form, *[2R-[2R*(4R*,8R*)]]-3,4-dihydro-2,5,7,8-methyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol tate, E-Vicotrat, Spondyvit, Tocopherex.* Crystals, mp $[\alpha]_D^{25}$ +0.25° (c = 10 in chloroform); $[\alpha]_D^{25}$ +3.2° (in etha

l-Form, crystals, mp 23°. $[\alpha]_D^{25}$ −2.0° (in ethanol).

Note: The international unit of vitamin E is equal to mg of standard *dl*-α-tocopheryl acetate. The *d*-form is t active: 1 mg = 1.36 I.U. *l*-α-Tocopheryl acetate has of the activity of *d*-α-tocopheryl acetate in the rat hemo test. Based on this activity a potency ratio of 1.4:1.0 *d*-α-tocopheryl acetate compared to *dl*-α-tocopheryl ace has been established.

THERAP CAT: Vitamin.

THERAP CAT (VET): Vitamin.

10161. Vitamin K. General term referring to a grou naphthoquinone derivatives required for the bioactivatio proteins involved in hemostasis. The designation "K" derived from the German "Koagulationsvitamin." Vita K compds are classified into 3 groups: *phylloquinone* (*q.v.*, found in green plants; *menaquinones* (K_2), *q.v.*, pri rily produced by intestinal bacteria; and *menadione* (*q.v.*, and derivatives which are synthetic, lipid soluble c pounds. Reduced *in vivo* to *dihydrovitamin K* (KH_2) serves as a coenzyme in the conversion of glutamic residues to γ-carboxyglutamic acid (Gla), *q.v.*, in the p translational modification of blood coagulation factor VII, IX and X, *q.q.v.*, and the anticoagulant proteins C S. Other Gla-containing proteins, such as the bone m protein, osteocalcin, *q.v.*, have been identified in a wide ety of tissues. This γ-carboxylation is accompanied by oxidation of KH_2 to *vitamin K epoxide* which is then cled back to vitamin K. Discovery: H. Dam, *Biochem* **215**, 475 (1929); **220**, 158 (1930); *Nature* **135**, 652 (19 Historical survey: H. Dam, *Vit. Horm.* **24**, 295-306 (19 Menadione and phylloquinone are metabolized by

FILE 'HCAPLUS' ENTERED AT 16:22:05 ON 11 FEB 2004

FILE COVERS 1907 - 11 Feb 2004 VOL 140 ISS 7
FILE LAST UPDATED: 10 Feb 2004 (20040210/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CELECOXIB/CN
L4           662 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L1(L)THU/RL
L5            92 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L1(L)(?CANCER? OR ?TUMOR? OR
                 ?NEOPLAS?)
L6            86 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L4 AND L5
L7            12 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L6 AND REVIEW/DT
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Celecoxib for cancer treatment

```
=> d que l10
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ATORVASTATIN/CN
L8           903 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L2(L)THU/RL
L9            12 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L2(L)(?CANCER? OR ?TUMOR? OR
                 ?NEOPLAS?)
L10           12 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L8 AND L9
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Atorvastatin for cancer treatment

```
=> d que l14
L3             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYSTINE/CN
L12          211 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L3(L)THU/RL
L13          103 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L3(L)(?CANCER? OR ?TUMOR? OR
                 ?NEOPLAS?)
L14           10 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L12 AND L13
```

Cystine for cancer treatment

```
=> d que l29
L20         1659 SEA FILE=HCAPLUS ABB=ON   PLU=ON  CYCLOOXYGENASE 2+PFT/CT(L)(ANT
                 AG? OR INHIB? OR BLOCK?)
L21            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "CYCLOOXYGENASE 2"/CN
L23         1659 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21(L)(ANTAG? OR INHIB? OR
                 BLOCK?)
L24         1659 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L20 OR L23
L25          606 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21(L)(?CANCER? OR ?TUMO? OR
```

```
                ?NEOPLAS?)
L26          247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND L25
L28          279 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21(L)(THU OR BAC OR DMA OR
                 PAC OR PKT)/RL
L29           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L28
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Cox-2 inhibitor to treat Cancer

```
=> d que l37
L22           13 SEA FILE=REGISTRY ABB=ON  PLU=ON  HMG-COA REDUCTASE?/CN
L32          371 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYDROXYMETHYLGLUTARYL-COA
                 REDUCTASE+PFT/CT(L)(INHIB? OR ANTAG? OR BLOCK?)
L33         3141 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22(L)(INHIB? OR ANTAG? OR
                 BLOCK?)
L34         3141 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 OR L33
L35          125 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22(L)(?CANCER? OR ?NEOPLAS?
                 OR ?TUMO?)
L36           86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND L35
L37            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND REVIEW/DT
```

HMG-CoA reductase inhib. to treat Cancer

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=> d que l38
L20         1659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CYCLOOXYGENASE 2+PFT/CT(L)(ANT
                 AG? OR INHIB? OR BLOCK?)
L21            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "CYCLOOXYGENASE 2"/CN
L22           13 SEA FILE=REGISTRY ABB=ON  PLU=ON  HMG-COA REDUCTASE?/CN
L23         1659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21(L)(ANTAG? OR INHIB? OR
                 BLOCK?)
L24         1659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 OR L23
L25          606 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21(L)(?CANCER? OR ?TUMO? OR
                 ?NEOPLAS?)
L26          247 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND L25
L35          125 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22(L)(?CANCER? OR ?NEOPLAS?
                 OR ?TUMO?)
L38           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L35
```

Cox-2 and HMG-CoA Red. Th. Combo. to Treat cancer

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=> d ibib ab 17 1-
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:1005865  HCAPLUS
TITLE:                    Cyclooxygenase inhibition and mechanisms of colorectal
                          cancer prevention
AUTHOR(S):                Chan, Timothy A.
CORPORATE SOURCE:         Sidney Kimmel Cancer Center, Johns Hopkins School of
                          Medicine, Baltimore, MD, 21231, USA
SOURCE:                   Current Cancer Drug Targets (2003), 3(6), 455-463
                          CODEN: CCDTB9; ISSN: 1568-0096
PUBLISHER:                Bentham Science Publishers Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  Colorectal cancer is a leading cause of cancer death throughout
     the world.  The high prevalence and mortality assocd. with colon cancer
     make effective prevention and treatment an important public health and
     economic concern.  Among the few agents known to inhibit colorectal
     tumorigenesis are the nonsteroidal anti-inflammatory drugs or NSAIDs, as
     well as newer agents such as celecoxib and rofecoxib.  Both epidemiol.
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celecoxib

studies and investigations with animals show that these compds. possess marked anti-colorectal cancer properties. NSAIDS are widely known to be inhibitors of the cyclooxygenase (COX) enzymes, and it is thought that the chemopreventive effects of NSAIDs are at least in part due to this ability to inhibit COX. More recent studies, however, have suggested that NSAIDs may also exert anti-cancer effects through mechanisms independent of COX inhibition. COX-dependent and COX-independent mechanisms are not mutually exclusive and it is likely that both are involved in the biol. activity of NSAIDs.

L7 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:919948 HCAPLUS
DOCUMENT NUMBER: 139:390535
TITLE: Use of NSAIDs for the chemoprevention of colorectal cancer
AUTHOR(S): Herendeen, Jill M.; Lindley, Celeste
CORPORATE SOURCE: Drug Development Fellow, University of North Carolina School of Pharmacy, Chapel Hill, NC, USA
SOURCE: Annals of Pharmacotherapy (2003), 37(11), 1664-1674
CODEN: APHRER; ISSN: 1060-0280
PUBLISHER: Harvey Whitney Books Co.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. OBJECTIVE: To discuss the role of nonsteroidal antiinflammatory drugs (NSAIDs) in the chemoprevention of colorectal cancer. DATA SOURCES: A MEDLINE search (1966-May 2003) was performed to identify key literature. Search items included, but were not limited to, NSAIDs, colorectal cancer, chemoprevention, cyclooxygenase-2 (COX-2)-specific inhibitors, and familial adenomatous polyposis (FAP). STUDY SELECTION AND DATA Extn.: The search included exptl. (in vitro and animal models) and clin. studies evaluating the use of NSAIDs for the chemoprevention of colorectal cancer. The MEDLINE search was supplemented by refs. from selected articles. DATA SYNTHESIS: Numerous exptl., epidemiol., and clin. studies suggest that NSAIDs have promise as anticancer agents. The mechanism by which NSAIDs lead to decreased colon carcinogenesis is not fully understood, but may involve restoration of apoptosis and inhibition of prostaglandin-mediated angiogenesis. Compelling evidence from many observational studies has consistently documented a 40-50% redn. in the risk of adenomatous polyps, colorectal cancer incidence, and mortality in patients using NSAIDs. Recent randomized, controlled trials have demonstrated a benefit with aspirin in reducing the rate of development of new or recurrent adenomas in high-risk patients. In addn., randomized studies using sulindac and celecoxib in patients with FAP have documented significant regression of existing adenomatous polyps. CONCLUSIONS: Inhibition of COX-2 is an example of a targeted approach to the chemoprevention of colorectal cancer. However, controversy exists about the safety, efficacy, and optimal treatment regimen of NSAIDs as long-term chemopreventive agents in the general population. Ongoing studies in high-risk patients with both selective and nonselective COX inhibitors will provide important information in the area of colorectal chemoprevention, but clin. trials' use of adenomas as surrogate markers for chemoprevention trials makes their application to the general population limited.
REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:552622 HCAPLUS
DOCUMENT NUMBER: 139:357796
TITLE: The medicinal chemistry implications of the anticancer effects of aspirin and other NSAIDs
AUTHOR(S): Gardiner, P. S.; Gilmer, J. F.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, School of Pharmacy, Trinity College, Dublin, Ire.
SOURCE: Mini-Reviews in Medicinal Chemistry (2003), 3(5), 461-470
CODEN: MMCIAE; ISSN: 1389-5575
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The regular intake of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) was assocd. with decreased incidence of certain types of cancer particularly those with an inflammatory component. The protective effects of these drugs in colorectal cancer are particularly marked, with a 40-50% redn. in risk. Research in this area has focussed on understanding and optimizing these cytoprotective effects. NSAIDs are believed to operate by inhibiting COX-2, an enzyme that appears to be involved in a no. of cancer promoting processes. This hypothesis is consistent with the observation that the COX-2 selective inhibitors dramatically decrease tumor formation in human and animal studies. Surprisingly aspirin, which is selective for COX-1 over COX-2, and sulindac, which is an equipotent inhibitor of the COX isoenzymes, appear to have a similar anticancer profile to the COX-2 selective NSAIDs. A no. of mechanisms were proposed to explain the anomalous effects of aspirin. The 1st of these relates to the unique mode of action of aspirin, which acetylates the COX-2 enzyme and generates the cancer-suppressing 15R-hydroxyeicosatetraenoic acid at the site of a potential tumor. The alternative rationale relates to the metab. of aspirin to salicylic acid, which has a cyclooxygenase independent anti-inflammatory mechanism, preventing the inflammatory response at the gene transcription level. A new generation of drugs could evolve from approaches to improving the therapeutic index of aspirin or by modifications to known therapies such as sulindac and celecoxib.

REFERENCE COUNT: 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:62276 HCAPLUS
DOCUMENT NUMBER: 138:313726
TITLE: Cyclooxygenase 2: a molecular target for cancer prevention and treatment
AUTHOR(S): Subbaramaiah, Kotha; Dannenberg, Andrew J.
CORPORATE SOURCE: Dept of Medicine, Weill Medical College of Cornell University, New York, NY, 10021, USA
SOURCE: Trends in Pharmacological Sciences (2003), 24(2), 96-102
CODEN: TPHSDY; ISSN: 0165-6147
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Cyclooxygenase 2 (COX-2), an inducible prostaglandin G/H synthase, is overexpressed in several human cancers. Here, the potential utility of selective COX-2 inhibitors in the prevention and treatment of

cancer is considered. The mechanisms by which COX-2 levels increase in cancers, key data that indicate a causal link between increased COX-2 activity and tumorigenesis, and possible mechanisms of action of COX-2 are discussed. In a proof-of-principle clin. trial, treatment with the selective COX-2 inhibitor celecoxib reduced the no. of colorectal polyps in patients with familial adenomatous polyposis. Selective COX-2 inhibitors appear to be sufficiently safe to permit large-scale clin. testing and numerous clin. trials are currently under way to det. whether selective inhibitors of COX-2 are effective in the prevention and treatment of cancer.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:542001 HCAPLUS
DOCUMENT NUMBER: 138:117080
TITLE: Novel approaches for colon cancer prevention by cyclooxygenase-2 inhibitors
AUTHOR(S): Reddy, Bandaru S.; Rao, Chinthalapally V.
CORPORATE SOURCE: Nutritional Carcinogenesis and Chemoprevention Program, American Health Foundation, Valhalla, NY, 10595, USA
SOURCE: Journal of Environmental Pathology, Toxicology and Oncology (2002), 21(2), 155-164
CODEN: JEPOEC; ISSN: 0731-8898
PUBLISHER: Begell House, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. During recent years, multidisciplinary studies in epidemiol. and mol. biol., as well as preclin. studies, have contributed much to our understanding of the etiol. of colorectal cancer; more importantly they have enabled us to approach its prevention. An impressive body of epidemiol. data suggests an inverse relationship between colorectal cancer risk and regular use of nonsteroidal antiinflammatory drugs (NSAIDs), including aspirin. Clin. trials with NSAIDs have demonstrated that NSAID treatment caused regression of preexisting colon adenomas in patients with familial adenomatous polyposis. Preclin. efficacy studies have provided compelling evidence that several phytochems. with antiinflammatory properties and NSAIDs act to retard, block, or reverse colon carcinogenesis. Equally exciting are opportunities for effective chemoprevention with selective cyclooxygenase-2 (COX-2) inhibitors including celecoxib and rofecoxib in a variety of preclin. models of colon cancer. Naturally occurring COX-2 inhibitors such as curcumin and certain phytosterols have been proven to be effective as chemopreventive agents against colon carcinogenesis with minimal gastrointestinal toxicity. Multistep process of carcinogenesis has provided substantial insights into the mechanisms by which naturally occurring and synthetic antiinflammatory agents modulate these events leading to suppression of tumorigenesis. Growing knowledge in this area has brought about innovative approaches using a combination of agents with different modes of action as a means of increasing efficacy and minimizing toxicity. The natural history of colorectal cancer, from dysplastic aberrant crypts to adenomas and adenocarcinomas, offers multiple opportunities for assessment and intervention. Of further importance would be to identify mol. targets that are crit. in the growth and survival of the malignant colorectal cell and are modulated by NSAIDs and COX-2 inhibitors.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:542000 HCAPLUS
DOCUMENT NUMBER: 138:117079
TITLE: COX-2 and prostanoid receptors: good targets for chemoprevention
AUTHOR(S): Kawamori, Toshihiko; Wakabayashi, Keiji
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center Research Institute, Tokyo, 104-0045, Japan
SOURCE: Journal of Environmental Pathology, Toxicology and Oncology (2002), 21(2), 149-153
CODEN: JEPOEC; ISSN: 0731-8898
PUBLISHER: Begell House, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Accumulating evidence indicates that COX-2 inhibitors are involved in colon and breast cancer development. Our previous studies indicated that nimesulide and celecoxib, selective COX-2 inhibitors, show inhibitory effects of intestinal carcinogenesis in azoxymethane-treated rats and mice and in Min mice models. We recently found that nimesulide suppressed PhIP-induced breast cancer in female SD rats in which COX-2 protein was over-expressed. These results led us to investigate the effects of prostaglandin E2 (PGE2) in the target tissues. PGE2 showed its biol. activity through binding to its membrane receptors, EP1-4. We also investigated the effects of EP receptors on colon carcinogenesis. We used receptor knockout mice and selective receptor antagonists. Our results indicated that the EP1 receptor plays a pivotal role in colon carcinogenesis. Selective EP1 receptor antagonists may be a new class of chemopreventive agents against colon cancer.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:420021 HCAPLUS
DOCUMENT NUMBER: 138:32606
TITLE: Inhibition of tumor angiogenesis by non-steroidal anti-inflammatory drugs: emerging mechanisms and therapeutic perspectives
AUTHOR(S): Dormond, Olivier; Ruegg, Curzio
CORPORATE SOURCE: Centre Pluridisciplinaire d'Oncologie (CePO), University of Lausanne Medical School, Lausanne, CH-1011, Switz.
SOURCE: Drug Resistance Updates (2001), 4(5), 314-321
CODEN: DRUPFW; ISSN: 1368-7646
PUBLISHER: Harcourt Publishers Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Chronic intake of non steroidal anti-inflammatory drugs (NSAIDs) is assocd. with a reduced risk of developing gastrointestinal tumors, in particular colon cancer. Increasing evidence indicates that NSAID exert tumor-suppressive activity on pre-malignant lesions (polyps) in humans and on established exptl. tumors in mice. Some of the tumor-suppressive effects of NSAIDs depend on the inhibition of cyclooxygenase-2 (COX-2), a key enzyme in the synthesis of prostaglandins and thromboxane, which is highly expressed in inflammation and cancer. Recent findings indicate that NSAIDs exert their anti-tumor effects by

suppressing tumor angiogenesis. The availability of COX-2-specific NSAIDs opens the possibility of using this drug class as anti-angiogenic agents in combination with chemotherapy or radiotherapy for the treatment of human cancer. Here we will briefly review recent advances in the understanding of the mechanism by which NSAIDs suppress tumor angiogenesis and discuss their potential clin. application as anti-cancer agents.
REFERENCE COUNT: 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:41667 HCAPLUS
DOCUMENT NUMBER: 136:256597
TITLE: Celecoxib as adjunctive therapy for treatment of colorectal cancer
AUTHOR(S): North, Ginnie Lee T.
CORPORATE SOURCE: School of Pharmacy, University of Montana, Missoula, MT, USA
SOURCE: Annals of Pharmacotherapy (2001), 35(12), 1638-1643
CODEN: APHRER; ISSN: 1060-0280
PUBLISHER: Harvey Whitney Books Co.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. OBJECTIVE: To describe the role of celecoxib as adjunctive therapy in the treatment of familial adenomatous polyposis (FAP), an inherited autosomal dominant predisposition syndrome for colorectal cancer. DATA SOURCES: Literature was evaluated through MEDLINE search (1995-Mar. 2000) and through secondary sources, using the search terms celecoxib, cyclooxygenase-2 inhibitors, and familial adenomatous polyps. DATA SYNTHESIS: Observational studies have found a decreased rate of colorectal cancer in people who regularly took aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs). The Food and Drug Administration granted accelerated approval in Dec. 1999 for the NSAID celecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, for adjunctive therapy in patients with FAP, based on a six-month, randomized, controlled clin. trial. CONCLUSIONS: Aspirin and other NSAIDs reduce the incidence of colorectal cancer in the general population. Limited clin. studies in patients with FAP using nonaspirin NSAIDs have shown a redn. in polyp burden. A current clin. trial using celecoxib has also shown a redn. in polyp burden in patients with FAP. The long-term clin. impact of using a selective COX-2 inhibitor is not known, since celecoxib has not been studied beyond six months in patients with FAP. By reducing the polyp burden in FAP patients, celecoxib may be useful as adjunctive chemotherapy, in addn. to routine endoscopic surveillance and surgery.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:16667 HCAPLUS
DOCUMENT NUMBER: 137:103189
TITLE: COX-2 inhibition and prevention of cancer
AUTHOR(S): Giercksky, Karl-Erik
CORPORATE SOURCE: Department of Surgical Oncology, The University of Oslo, Oslo, Norway
SOURCE: Best Practice & Research, Clinical Gastroenterology (2001), 15(5), 821-833
CODEN: BPRCB6

PUBLISHER: Bailliere Tindall
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. The potential for cyclooxygenase inhibition in cancer prevention and treatment is founded on epidemiol. (redn. of colorectal cancer in aspirin users), animal expts. and mol. genetics. Trials using the NSAID sulindac also reduced the no. of polyps in patients with familial adenomatous polyposis, but the well-known gastrointestinal toxic effects of aspirin and NSAIDs have discouraged the exploitation of their antineoplastic potential. The advent of specific COX-2 inhibitors, which do not interfere with the cytoprotective constitutive COX-1 enzyme, and the demonstration of increased COX-2 expression in many common malignancies beside colorectal cancer, has opened up new therapeutic possibilities. Recently a non-cyclooxygenase effect of COX-2 inhibitors, which combines the PPAR.delta. and the APC tumor suppressor activity, was also demonstrated. The selective COX-2 inhibitor celecoxib has been approved by the FDA for adjuvant treatment of familial adenomatous polyposis, and a large no. of prevention and treatment trials of colorectal and other common cancers (prostate and breast cancer) have been started.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:649750 HCAPLUS
DOCUMENT NUMBER: 136:318627
TITLE: Familiar drugs may prevent cancer
AUTHOR(S): Sharma, R. A.; Gescher, A. J.; O'Byrne, K. J.; Steward, W. P.
CORPORATE SOURCE: Oncology Department, University of Leicester, Leicester, LE1 5WW, UK
SOURCE: Postgraduate Medical Journal (2001), 77(910), 492-497
CODEN: PGMJAO; ISSN: 0032-5473
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Despite pos. results in large scale chemoprevention trials, many physicians are unaware of the potential cancer preventive properties of drugs in common usage. The antiestrogen tamoxifen and the selective cyclooxygenase-2 inhibitor celecoxib have been licensed in the USA for the chemoprevention of breast and colorectal cancers, resp., in selected high risk individuals. Similarly, folate and retinol have been shown to decrease the incidence of colorectal cancer and squamous cell carcinoma of the skin resp. in large scale intervention trials. Other retinoids have proved efficacious in the tertiary chemoprevention of cancers of the breast and head/neck. Epidemiol. evidence also exists in favor of aspirin, non-steroidal anti-inflammatory drugs, and angiotensin converting enzyme inhibitors preventing certain cancers. Phytochems. may represent less toxic alternatives to these agents. Although some of these drugs are available without prescription and most are not yet licensed for use in cancer chemoprevention, physicians and students of medicine should be aware of this accumulating evidence base. Practitioners should be amenable to patient referral to discuss complex issues such as risk estn. or potential benefit from intervention.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:566978 HCAPLUS
DOCUMENT NUMBER: 136:272452
TITLE: Cyclooxygenase-2: a target for the prevention and treatment of breast cancer
AUTHOR(S): Howe, L. R.; Subbaramaiah, K.; Brown, A. M. C.; Dannenberg, A. J.
CORPORATE SOURCE: Strang Cancer Research Laboratory, Rockefeller University, New York, NY, 10021, USA
SOURCE: Endocrine-Related Cancer (2001), 8(2), 97-114
CODEN: ERCAE9; ISSN: 1351-0088
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Cyclooxygenase-2 (COX-2), an inducible prostaglandin synthase, is normally expressed in parts of the kidney and brain. Aberrant COX-2 expression was first reported in colorectal carcinomas and adenomas, and has now been detected in various human cancers, including those of the breast. Strikingly, COX-2 overexpression in murine mammary gland is sufficient to cause tumor formation. To date, the role of COX-2 in tumorigenesis has been most intensively studied in the colon. Thus, the relationship between COX-2 and neoplasia can best be illustrated with ref. to intestinal tumorigenesis. Here we consider the potential utility of selective COX-2 inhibitors for the prevention and treatment of breast cancer. Data for cancers of the colon and breast are compared where possible. In addn., the mechanisms by which COX-2 is upregulated in cancers and contributes to tumorigenesis are discussed. Importantly, several recent studies of mammary tumorigenesis in animal models have found selective COX-2 inhibitors to be effective in the prevention and treatment of breast cancer. Clin. trials will be needed to det. whether COX-2 inhibition represents a useful approach to preventing or treating human breast cancer.
REFERENCE COUNT: 176 THERE ARE 176 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:527319 HCAPLUS
DOCUMENT NUMBER: 135:298050
TITLE: Chemoprevention of colorectal cancer
AUTHOR(S): Clapper, Margie L.; Chang, Wen-Chi L.; Meropol, Neal J.
CORPORATE SOURCE: Divisions of Population Science, Fox Chase Cancer Center, Philadelphia, PA, 19111, USA
SOURCE: Current Opinion in Oncology (2001), 13(4), 307-313
CODEN: CUOOE8; ISSN: 1040-8746
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with refs. Chemopreventive strategies hold substantial promise for reducing the incidence of colorectal cancer, the second leading cause of cancer-related mortality in the United States. This review focuses on recent advances in the identification of mol. targets and novel strategies for chemopreventive intervention. Many clin. trials are now in progress to assess the ability of synthetic agents or nutritional supplements to alter either the no. of colorectal adenomas or biomarkers assocd. with colorectal tumorigenesis. Populations under study include genetically

defined high-risk people and those with increased risk based on a personal history of colorectal neoplasia. A recent study showing that celecoxib, a cyclooxygenase-2 inhibitor, can alter the natural history of polyp formation in patients with familial adenomatous polyposis has provided a benchmark for the clin. development of other chemopreventive agents and heightened awareness that colorectal cancer is a preventable disease.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib ab 110 1-1
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

Atorvastatin

L10 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:991029 HCAPLUS
DOCUMENT NUMBER: 140:23224
TITLE: Interferon-statin combination therapy
INVENTOR(S): Cantrell, Stephen B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232033	A1	20031218	US 2003-370434	20030220

PRIORITY APPLN. INFO.: US 2002-359265P P 20020221
AB A method for pharmacol. treatment of cancer and other diseases is presented which includes the novel combination of a statin (Hmg-CoA reductase inhibitor, such as lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, pravastatin, or newer agents), with an interferon (such as interferon alfa-2 b or others) or an angiogenesis inhibitor (a very similar and often overlapping group of drugs which inhibit blood vessel growth and maintenance, such as thalidomide, angiostatin, endostatin, or other agents), and also including concurrent administration of selenium and calcium. The method disclosed in this invention is useful because it can prove more effective than previously known therapies for certain diseases and because its use may be more tolerable, less disfiguring, and less expensive than other methods. The method here disclosed can be readily reproduced by any person skilled in the art of treating disease.

L10 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:836869 HCAPLUS
DOCUMENT NUMBER: 139:302031
TITLE: Methods using polyene macrolide antibiotics and cholesterol-lowering agents for the treatment of cancer
INVENTOR(S): Solomon, Keith R.
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086418	A1	20031023	WO 2003-US10972	20030410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-371897P P 20020411

AB The invention provides a method for treating a mammalian tumor/cancer using a polyene macrolide antibiotic selected from the group consisting of filipin, candicidin, pimaricin, nystatin, etruscomycin and candidin. In a preferred embodiment, the method further comprises administration of a cholesterol-lowering agent.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:236808 HCAPLUS
DOCUMENT NUMBER: 139:94967
TITLE: Statins can inhibit proliferation of human breast cancer cells in vitro
AUTHOR(S): Seeger, H.; Wallwiener, D.; Mueck, A. O.
CORPORATE SOURCE: Section of Gynecological Endocrinology and Menopause, Department of Obstetrics and Gynecology, University of Tuebingen, Germany
SOURCE: Experimental and Clinical Endocrinology & Diabetes (2003), 111(1), 47-48
CODEN: ECEDFQ; ISSN: 0947-7349
PUBLISHER: J. A. Barth Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of five statins, i.e. atorvastatin, fluvastatin, lovastatin, pravastatin and simvastatin was investigated on the proliferation of the human breast cancer cell line MCF-7. All statins except of pravastatin were able to inhibit cell proliferation up to 90% at a concn. of 50 .mu.M. Between the effective statins no significant difference was obsd. indicating a class-specific effect. These data suggest that statins may have clin. significance in the primary prevention of human breast cancer beyond their cholesterol-lowering effect. However, clin. proof must be awaited before drawing any further conclusions.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:133048 HCAPLUS
DOCUMENT NUMBER: 138:163519
TITLE: Improved treatment of cancer with irinotecan based on

genotyping of human gene MDR1 encoding P-glycoprotein
INVENTOR(S): Heinrich, Guenther; Kerb, Reinhold
PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013535	A2	20030220	WO 2002-EP8220	20020723
WO 2003013535	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-117608 A 20010723
EP 2002-11710 A 20020524

AB The present invention relates to the use of irinotecan or a deriv. thereof for the prepn. of a pharmaceutical compn. for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with variant alleles of genes involved in irinotecan metab., and in particular the multidrug resistance gene MDR1. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addn. and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calcd. based on genotype correlated with the risk of toxic reaction.

L10 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:777730 HCAPLUS
DOCUMENT NUMBER: 137:299915
TITLE: Farnesyl transferase inhibitors in combination with HMG CoA reductase inhibitors for the inhibition for the treatment of cancer
INVENTOR(S): Kajiji, Shama M.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078706	A1	20021010	WO 2002-US9751	20020329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002151563	A1	20021017	US 2002-103251	20020321

PRIORITY APPLN. INFO.: US 2001-279965P P 20010329
OTHER SOURCE(S): MARPAT 137:299915

AB This invention relates to pharmaceutical compns. for the treatment of abnormal cell growth, such as cancer or benign hyperproliferative disorder, in a mammal, which comprises a therapeutically effective amt. of farnesyl transferase (Ftase) inhibitor in combination with an hydroxymethylglutaryl CoA (HMG CoA) reductase inhibitor and a pharmaceutically acceptable carrier.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:597795 HCAPLUS
DOCUMENT NUMBER: 135:185456
TITLE: Tumor necrosis factor (TNF-.alpha.) inhibitors
INVENTOR(S): Sugiyama, Yasuo; Odaka, Hiroyuki; Naruo, Ken-ichi; Funatsu, Masami; Ikeya, Kazuaki; Suzuki, Yoshiharu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058443	A1	20010816	WO 2001-JP881	20010208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001032245	A5	20010820	AU 2001-32245	20010208
EP 1275388	A1	20030115	EP 2001-904345	20010208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2001294526	A2	20011023	JP 2001-33761	20010209
US 2003018040	A1	20030123	US 2002-203292	20020808

PRIORITY APPLN. INFO.: JP 2000-38266 A 20000210

WO 2001-JP881 W 20010208

AB TNF-inhibitors contg. at least one compd. selected from the group consisting of cerivastatin, atorvastatin, simvastatin, pravastatin, itavastatin and (+)-(3R,5S)-7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methanesulfonylamino) pyrimidin-5-yl]-3,5-dihydroxy-6(E)-heptenoic acid and salts thereof which have sufficiently favorable properties as drugs, for example, exhibiting excellent preventive and therapeutic effects on TNF-.alpha.-assocd. diseases such as inflammatory diseases without showing any side effects.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:572695 HCAPLUS
DOCUMENT NUMBER: 136:272766
TITLE: Cerivastatin triggers tumor-specific apoptosis with higher efficacy than lovastatin
AUTHOR(S): Wong, W. Wei-Lynn; Tan, Melissa M.; Xia, Zhenlei; Dimitroulakos, Jim; Minden, Mark D.; Penn, Linda Z.
CORPORATE SOURCE: Department of Cellular and Molecular Biology, University Health Network, Toronto, ON, M5G 2M9, Can.
SOURCE: Clinical Cancer Research (2001), 7(7), 2067-2075
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The statin family of drugs inhibits 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, the rate-limiting enzyme of the mevalonate pathway, and is used clin. as a safe and effective approach in the control of hypercholesterolemia. We have shown previously (Dimitroulakos, J., Nohynek, D., Backway, K. L., Hedley, D. W., Yeger, H., Freedman, M. H., Minden, M D., and Penn, L. Z.) increased sensitivity of acute myelogenous leukemias to lovastatin-induced apoptosis: a potential therapeutic approach. Blood, 93: 1308-1318, 1999, that lovastatin, a prototypic member of the statin family, can induce apoptosis of human acute myeloid leukemia (AML) cells in a sensitive and specific manner. In the present study, we evaluated the relative potency and mechanism of action of the newer synthetic statins, fluvastatin, atorvastatin, and cerivastatin, to trigger tumor-specific apoptosis. Cerivastatin is at least 10 times more potent than the other statins at inducing apoptosis in AML cell lines. Cerivastatin-induced apoptosis is reversible with the addn. of the immediate product of the HMG-CoA reductase reaction, mevalonate, or with a distal product of the pathway, geranylgeranyl pyrophosphate. This suggests protein geranylgeranylation is an essential downstream component of the mevalonate pathway for cerivastatin similar to lovastatin-induced apoptosis. The enhanced potency of cerivastatin expands the no. of AML patient samples as well as the types of malignancies, which respond to statin-induced apoptosis with acute sensitivity. Cells derived from acute lymphocytic leukemia are only weakly sensitive to lovastatin cytotoxicity but show robust response to cerivastatin. Importantly, cerivastatin is not cytotoxic to nontransformed human bone marrow progenitors. These results strongly support the further testing of cerivastatin as a novel anticancer therapeutic alone and in combination with other agents in vivo.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:114844 HCAPLUS
DOCUMENT NUMBER: 134:173034
TITLE: Analog, antagonist or agonist of caveolin-1 as medicament for the prevention and/or the treatment of ischemic heart and peripheral vascular diseases, tumor and wounds
INVENTOR(S): Feron, Olivier; Balligand, Jean-Luc
PATENT ASSIGNEE(S): Universite Catholique de Louvain, Belg.
SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1076091	A1	20010214	EP 1999-870171	19990809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001011038	A2	20010215	WO 2000-EP7731	20000809
WO 2001011038	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1206539	A2	20020522	EP 2000-951488	20000809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2002156123	A1	20021024	US 2002-68965	20020211

PRIORITY APPLN. INFO.: EP 1999-870171 A 19990809
WO 2000-EP7731 W 20000809

AB The present invention aims at the restoration of a physiol. prodn. of nitric oxide (NO) in endothelial cells, particularly in a target dysfunctional endothelium. NO is produced by calmodulin dependent enzyme, the endothelial isoform nitric oxide synthase (eNOS). Caveolin, the structural protein of caveolae, serves as a competitive inhibitor of calmodulin-dependent activation of eNOS. The present invention provides a method of screening of new compds. which may be analogs, agonists or antagonists of caveolin-1 to its active site(s) upon the eNOS or other mols. such as kinases. The present invention is related to the use of a compd. or a pharmaceutical compn. for the prevention and/or the treatment of ischemic heart and peripheral vascular diseases including cerebral diseases, tumor development and wound healing.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:209913 HCAPLUS
DOCUMENT NUMBER: 132:260674
TITLE: A method of treating cancer using an HMG-CoA reductase inhibitor and a farnesyl-protein transferase inhibitor

INVENTOR(S): Graham, Samuel L.; Heimbrook, David C.; Koblan, Kenneth S.; Oliff, Allen I.; Stirdivant, Steven M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000016778	A1	20000330	WO 1999-US21773	19990923
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962564	A1	20000410	AU 1999-62564	19990923

PRIORITY APPLN. INFO.: US 1998-101633P P 19980924
GB 1998-24554 A 19981109
WO 1999-US21773 W 19990923

AB The invention provides a method of treating cancer which comprises administering to a mammal a compn. which comprises an HMG-CoA reductase inhibitor and a farnesyl-protein transferase (FPT) inhibitor. Prepn. of FPT inhibitors is described.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:209829 HCAPLUS
DOCUMENT NUMBER: 132:260673
TITLE: A method of treating cancer using inhibitors of HMG-CoA reductase and prenyl-protein transferase
INVENTOR(S): Graham, Samuel L.; Koblan, Kenneth S.; Heimbrook, David C.; Oliff, Allen I.; Stirdivant, Steven M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000016626	A1	20000330	WO 1999-US22224	19990923
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9961624 A1 20000410 AU 1999-61624 19990923

PRIORITY APPLN. INFO.: US 1998-101623P P 19980924
GB 1998-24575 A 19981109
WO 1999-US22224 W 19990923

AB A method of treating cancer comprises administering to a mammal a compn. contg. a first compd. which is an HMG-CoA reductase inhibitor and a second compd. which is a prenyl-protein transferase inhibitor, and which is efficacious in vivo as an inhibitor of the growth of cancer cells characterized by a mutated K4B-Ras protein. For example, 1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)imidazolylmethyl]-2-piperazinone dihydrochloride was prepd. (among other compds.) and tested for the inhibitory activity against human farnesyl protein transferase; it was found to have IC50 of .ltoreq. 1 .mu.M.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:736664 HCAPLUS
DOCUMENT NUMBER: 131:346502
TITLE: Combinations of protein farnesyltransferase inhibitors and HMG-CoA reductase inhibitors and their use to treat cancer and other diseases
INVENTOR(S): Leopold, Judith; Newton, Roger Schofield
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958505	A2	19991118	WO 1999-US10188	19990510
WO 9958505	A3	20000106		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2331295	AA	19991118	CA 1999-2331295	19990510
AU 9939792	A1	19991129	AU 1999-39792	19990510
AU 758891	B2	20030403		
EP 1077949	A2	20010228	EP 1999-922898	19990510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9911785	A	20010403	BR 1999-11785	19990510
EE 200000660	A	20020415	EE 2000-660	19990510
JP 2002514628	T2	20020521	JP 2000-548309	19990510
NZ 508357	A	20020927	NZ 1999-508357	19990510
US 6492410	B1	20021210	US 2000-674818	20001106
ZA 2000006491	A	20020509	ZA 2000-6491	20001109

NO 2000005680	A	20010110	NO 2000-5680		20001110
HR 2000000771	A1	20010630	HR 2000-771		20001113
BG 105003	A	20010731	BG 2000-105003		20001129
PRIORITY APPLN. INFO.:			US 1998-85202P	P	19980512
			US 1998-92253P	P	19980710
			WO 1999-US10188	W	19990510

OTHER SOURCE(S): MARPAT 131:346502

AB Novel combinations of inhibitors of protein farnesyltransferase enzymes and HMG CoA reductases enzymes are described, as well as methods for the prepn. and pharmaceutical compns. of the same, which are useful in preventing or treating cancer, restenosis, psoriasis, endometriosis, atherosclerosis, or viral infections.

L10 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:9696 HCAPLUS
DOCUMENT NUMBER: 130:61066
TITLE: Farnesyl transferase inhibitors in combination with HMG-CoA reductase inhibitors for the treatment of cancer
INVENTOR(S): Kajiji, Shama Mohammed
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9857633	A1	19981223	WO 1998-IB881		19980605
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9874459	A1	19990104	AU 1998-74459		19980605
AU 724676	B2	20000928			
EP 986387	A1	20000322	EP 1998-921688		19980605
EP 986387	B1	20030402			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
BR 9810616	A	20000912	BR 1998-10616		19980605
JP 2000513031	T2	20001003	JP 1999-504030		19980605
AT 235905	E	20030415	AT 1998-921688		19980605
ZA 9805182	A	19991217	ZA 1998-5182		19980615
HR 980328	B1	20020630	HR 1998-980328		19980616
NO 9906206	A	20000215	NO 1999-6206		19991215
MX 9911798	A	20000630	MX 1999-11798		19991215
US 2003114503	A1	20030619	US 2002-217108		20020812
PRIORITY APPLN. INFO.:			US 1997-49638P	P	19970616
			WO 1998-IB881	W	19980605
			US 1999-367435	B1	19991025

OTHER SOURCE(S): MARPAT 130:61066

AB A method is provided for treating cancer in a mammal, including a human, which comprises administering to the mammal a farnesyl transferase inhibitor in combination with an HMG-CoA reductase inhibitor.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

cystine

L14 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:434341 HCAPLUS
DOCUMENT NUMBER: 139:924
TITLE: Combination of cimetidine and cysteine derivatives for treating cancer
INVENTOR(S): Weidner, Morten Sloth
PATENT ASSIGNEE(S): Astion Oncology A.P.S., Den.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045359	A2	20030605	WO 2002-DK792	20021126
WO 2003045359	A3	20031218		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003158118	A1	20030821	US 2002-303867		20021126
PRIORITY APPLN. INFO.:			DK 2001-1761	A	20011126
			DK 2002-1086	A	20020710
			US 2002-395344P	P	20020712

OTHER SOURCE(S): MARPAT 139:924
AB The present invention relates to new substances in the form of chem. complexes comprising cimetidine or a deriv. thereof and a cysteine deriv. and to compns. comprising said complexes or combination. The invention further relates to the therapeutic effect of such combinations in relation to treating cancer, cancer chemoprevention or the suppression of hypersensitivity and/or inflammatory reactions of a mammal. The antitumor affect on a complex of cimetidine and N-acetylcysteine (2:3 molar ratio) was demonstrated in mice.

L14 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:946829 HCAPLUS
DOCUMENT NUMBER: 138:13506
TITLE: Adjuvant immune therapy in the treatment of solid

tumors through modulation of signaling pathways following engagement of humoral and cell mediated-responses
INVENTOR(S): Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 263,486.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002187130	A1	20021212	US 2001-880745	20010613

PRIORITY APPLN. INFO.: US 2001-263486 A2 20010123

AB The inventors propose a compn. with immunogenic properties acting like an anti-cancer vaccine, method of treatment, and method of administration. The compn. is referred to as a cytokine modulator. The invention combines a novel combination with two esp. important aspects: first, the invention proposes to simultaneously stimulate response in white blood cells and a patient's tumor cells with a mitogen-challenging compd., preferably a lectin, in the preferred mode the selected lectin being phytohemagglutinin, and second, to generate heat shock protein. The method of manufg. proposed utilizes a system calcd. to better insure sterility and streamline prodn. of the cytokine modulator. A method of testing in conjunction with the therapy is also claimed utilizing clin. assessment of disease activity, patient performance status, and quality of life questionnaire. Should efficacy of a treatment fall off, particularly because of mutation or adaptation, the compn. and method may be re-applied. The invention is not limited to humans, and is applicable to other mammals. The compn. is usable as a stand-alone compn., but preferably is used in conjunction with std. therapy such as radiation, chemotherapy or surgery, particularly surgical therapy, and in conjunction with the administration of cystine, to enhance immune system competency.

L14 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:869587 HCAPLUS
DOCUMENT NUMBER: 137:346169
TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and an HMG-CoA inhibitor and cystine to enhance glutathione
INVENTOR(S): Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Pat. Appl. 2002 86,894.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169195	A1	20021114	US 2002-57511	20020126
US 2002086894	A1	20020704	US 2001-912703	20010725

US 6534540 B2 20030318
WO 2002028270 A2 20020411 WO 2001-US31328 20011006
WO 2002028270 A3 20020613
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-264511P P 20010126
US 2001-307689P P 20010725
US 2001-912703 A2 20010725
WO 2001-US31328 W 20011006
US 2000-238504P P 20001006
US 2000-238506P P 20001006
US 2000-243901P P 20001027
US 2000-243902P P 20001027
US 2000-245592P P 20001117
US 2001-263486P P 20010123

AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer, esp. prostate cancer, and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer, esp. prostate cancer, and a method of treatment of cancer by that combination, esp. prostate cancer. Also contemplated is the addn. of lipoic acid and compds. to maintain adequate levels of selenium, Vitamin C and Vitamin E. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristic of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer. A patient with stage 4 metastatic prostate cancer was treated with Vioxx and Mevacor.

L14 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:717053 HCAPLUS
DOCUMENT NUMBER: 137:226597
TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-a (HMG-CoA) reductase inhibitor
INVENTOR(S): Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of Appl. No. PCT/US01/31328.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2002132781 A1 20020919 US 2001-997490 20011117
US 2002086894 A1 20020704 US 2001-912703 20010725
US 6534540 B2 20030318
WO 2002028270 A2 20020411 WO 2001-US31328 20011006
WO 2002028270 A3 20020613
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002067853 A2 20020126 WO 2002-US2480 20020126
WO 2002067853 A3 20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002083124 A1 20021024 WO 2002-US2478 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002094021 A1 20021128 WO 2002-US2477 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-238504P P 20001006
US 2000-238506P P 20001006
US 2000-243901P P 20001027
US 2000-243902P P 20001027
US 2000-245592P P 20001103
US 2001-264511P P 20010126
US 2001-307689P P 20010725
US 2001-912703 P 20010725
WO 2001-US31328 W 20011006
US 2000-249592P P 20001117

US 2001-263486P P 20010123
US 2001-264504P P 20010126
US 2001-997490 A2 20011117
US 2002-352047P P 20020126

AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. Also contemplated is the addn. of lipoic acid and compds. to maintain adequate levels of selenium, vitamin C and vitamin E. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristics of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer.

L14 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:675772 HCAPLUS
DOCUMENT NUMBER: 137:195546
TITLE: Treatment of HIV and viral diseases, vascular disease and cancer using a COX-2 inhibitor and cystine
INVENTOR(S): Kindness, George; Schumm, Brooke, III; Guilford, Timothy F.
PATENT ASSIGNEE(S): Probiochem, LLC, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002067853 A2		20020906	WO 2002-US2480	20020126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR

PRIORITY APPLN. INFO.:
US 2000-PV238504 20001006
US 2000-PV238506 20001006
US 2000-PV243901 20001027
US 2000-PV243902 20001027
US 2000-PV245592 20001117
US 2001-PV264511 20010126
US 2001-PV264504 20010126
US 2001-PV307689 20010725
US 2001-912703 20010725
WO 2001-US31328 20011006
US 2001-997490 20011117

AB The invention discloses the combination of a selective COX-2 inhibitor and cystine for the treatment of anti-viral diseases, including HIV, immuno-compromised individuals, AIDS and hepatitis C, atherosclerosis and

related atherosclerosis vascular disease states, coronary ischemic syndrome, thrombosis, related vascular problems, cancer and to alleviate 5-hydroxy tryptamine- mediated mechanisms by at least relieving inflammatory symptoms, through regulation of cytokine activated responses, including migraine and migraine-like conditions, to ameliorate neurodegenerative diseases aggravated by inflammatory condition and carotidynia. An HMG-CoA reductase inhibitor may be added to enhance the combination. Magnesium sulfate or similar compd. is proposed to be added to enhance the treatment of neurodegenerative conditions.

L14 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:505414 HCAPLUS
DOCUMENT NUMBER: 137:57551
TITLE: Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-A (HMG-CoA) reductase inhibitor
INVENTOR(S): Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086894	A1	20020704	US 2001-912703	20010725
US 6534540	B2	20030318		
WO 2002028270	A2	20020411	WO 2001-US31328	20011006
WO 2002028270	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW				
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AU 2002013050	A5	20020415	AU 2002-13050	20011006
US 2002132781	A1	20020919	US 2001-997490	20011117
WO 2003022268	A1	20030320	WO 2001-US44050	20011117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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WO 2002067853	A2	20020126	WO 2002-US2480	20020126
WO 2002067853	A3	20021031		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
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GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002083124 A1 20021024 WO 2002-US2478 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002169195 A1 20021114 US 2002-57511 20020126
WO 2002094021 A1 20021128 WO 2002-US2477 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003162829 A1 20030828 US 2003-390517 20030317
PRIORITY APPLN. INFO.: US 2000-245592P P 20001117
US 2001-263486P P 20010123
US 2001-264511P P 20010126
US 2000-238504P P 20001006
US 2000-238506P P 20001006
US 2000-243901P P 20001027
US 2000-243902P P 20001027
US 2000-249592P P 20001117
US 2001-264504P P 20010126
US 2001-307689P P 20010725
US 2001-912703 A2 20010725
WO 2001-US31328 W 20011006
US 2001-997490 A2 20011117
US 2002-352047P P 20020126

AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristic of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer. An anticancer compn. comprises rofecoxib, lovastatin, and cystine.

L14 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:419718 HCAPLUS
DOCUMENT NUMBER: 131:73007
TITLE: Effects of D-methionine-containing solution on tumor cell growth in vitro
AUTHOR(S): Sasamura, Taizo; Matsuda, Akihiko; Kokuba, Yukifumi
CORPORATE SOURCE: Infusion Research Department, Medical Information Development Division, Hoechst Marion Roussel Ltd., Saitama, 350, Japan
SOURCE: Arzneimittel-Forschung (1999), 49(6), 541-543
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of a nutrition therapy with D-methionine (Met)-contg. soln. were investigated in cell cultures of the AH109A cell line. The growth of AH109A hepatoma cells in culture media with D-Met-supplemented medium, L-Met-supplemented medium (control) and Met-free medium was compared. The D-Met-supplemented medium inhibited the cell growth to an extent similar to that manifested in the Met-free medium. The total free amino acid concns. in the control medium decreased by approx. 40% on day 6 post-culture. However, the free amino acid concns. in D-Met-supplemented and Met-free media did not change. Furthermore, alanine, which was not added to RPMI-1640, was detected in the control medium on day 6 post-culture. These results suggest the possibility of application of D-Met-contg. soln. to cancer patients receiving total parenteral nutrition.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:650046 HCAPLUS
DOCUMENT NUMBER: 129:281005
TITLE: Nutritional products with high fat, low carbohydrate and amino acid imbalance
INVENTOR(S): Pellico, Michael A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817695	A	19981006	US 1997-997837	19971224
CA 2244608	C	20021217	CA 1998-2244608	19980731
CA 2244608	AA	19990624		
EP 925726	A1	19990630	EP 1998-308062	19981002
EP 925726	B1	20040128		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-997837 A 19971224
AB A nutritional product is provided for cancer patients comprising, as per caloric requirement, a low concn. of carbohydrate, a high concn. of fat

and an imbalance of amino acids wherein L-phenylalanine, L-tyrosine and L-methionine are present in the below normal concns. and L-leucine is present in substantial excess of normal concns. to suppress cancer growth and as an adjunct to conventional cancer therapies. For example, a product contained L-alanine 45, L-arginine.cntdot.HCl 60.5, L-aspartic acid 93.5, L-cystine 23, L-glutamic acid 339.5, glycine 52.5, L-histidine.cntdot.HCl 118, L-isoleucine 95, L-leucine 145.5, L-lysine.cntdot.HCl 118, L-methionine 47.5, L-phenylalanine 2, L-proline 177.5, L-serine 91, L-threonine 65, L-tryptophan 21.5, L-tyrosine 2250, L-valine 107, taurine 10, corn starch 100, sardine oil 915, lard 150, corn oil 500, cod liver oil 350, Alphacel nonnutritive bulk 1121, and ethoxiquin 1250 g.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:304022 HCAPLUS
DOCUMENT NUMBER: 124:333071
TITLE: Use of non-toxic cysteine sulfoxide derivatives in the treatment of cancer or for enhancing the T-cell count
INVENTOR(S): Holt, John Alfred Gorton
PATENT ASSIGNEE(S): Australia
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 705603	A1	19960410	EP 1995-306587	19950919
EP 705603	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 195419	E	20000915	AT 1995-306587	19950919
EP 764442	A1	19970326	EP 1996-306620	19960912
R: CH, DE, DK, FR, GB, IE, IT, LI, NL				
AU 9665682	A1	19970327	AU 1996-65682	19960918

PRIORITY APPLN. INFO.:
GB 1994-19061 A 19940920
AU 1995-31769 A 19950919
EP 1995-306587 A 19950919
US 1995-530745 A 19950919
GB 1996-3471 A 19960219

OTHER SOURCE(S): MARPAT 124:333071

AB A therapeutic method, applicable in vivo to a patient or in vitro to a transfusable body fluid or a transplantable body part, comprises administering to the patient, body fluid or body part an effective amt. of a non-toxic cysteine sulfoxide RSOCH2CH(NH2)CO2H (R = C1-4 alkyl, C2-4 alkenyl), and while said non-toxic cysteine sulfoxide is present administering to the patient, body fluid or body part an ED of microwave electromagnetic radiation of frequency in the range of about 400-450 MHz. The method is effective to treat cancers present in the patient, body fluid of body part, and in vivo to enhance T-cell count in an immunodeficient individual. Aq. solns. of t-Bu hydroperoxide (I) were prepd. by dissolving 50 mL of 70% aq. soln. of t-Bu hydroperoxide in 1 L of normal saline, then 15-30 mL of this soln. was given i.v. over a period of up to 15 min. Aq. solns. of Me cysteine sulfoxide (II) was prepd. by

dissolving 100 g in 1 L of normal saline, then 30-60 mL of this soln. was given i.v. The successful treatment of a patient suffering from adenosquamous carcinoma floor of the mouth with 15 day course of I and II is reported.

L14 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:681191 HCAPLUS
DOCUMENT NUMBER: 123:93144
TITLE: Formulation and characterization of polyterephthalamide microcapsules as carriers for the anticancer agent, 5-fluorouracil
AUTHOR(S): Sawant, Krutika K.; Murthy, R.S.R.
CORPORATE SOURCE: Faculty of Tech. & Engg., Kalabhavan, M.S. University of Baroda, Baroda, India
SOURCE: Indian Journal of Pharmaceutical Sciences (1994), 56(4), 117-20
CODEN: IJSIDW; ISSN: 0250-474X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyterephthalamide microcapsules were prepd. by interfacial polycondensation reaction between diamino acids and a diacid chloride. The formulation conditions were optimized by varying parameters like mode of emulsification, time of emulsification, concn. of emulsifying agent, time of polymn. and phase vol. ratio till microcapsules of desired particle size range were obtained. These microcapsules are suggested as carriers for the anticancer drug, 5-Fluorouracil, for the purpose of drug targeting.

=> s l29 or l37 or l38
L72 53 L29 OR L37 OR L38

=> b medline
FILE 'MEDLINE' ENTERED AT 16:23:58 ON 11 FEB 2004

FILE LAST UPDATED: 10 FEB 2004 (20040210/UP). FILE COVERS 1958 TO DATE.

On December 14, 2003, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http:\\www.nih.gov/pubs/yechbull/nd03/nd03_mesh.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l50
L44 163056 SEA FILE=MEDLINE ABB=ON PLU=ON ANTINEOPLASTIC AGENTS+PFT/CT
L48 8521 SEA FILE=MEDLINE ABB=ON PLU=ON CYCLOOXYGENASE INHIBITORS+PFT/CT
L49 292 SEA FILE=MEDLINE ABB=ON PLU=ON L48 AND L44
L50 77 SEA FILE=MEDLINE ABB=ON PLU=ON L49 AND REVIEW/DT

Cox-2 inhib. to treat cancer

=> d que l53

```
L44      163056 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+PFT/CT
L51        4556 SEA FILE=MEDLINE ABB=ON  PLU=ON  HYDROXYMETHYLGLUTARYL-COA
                REDUCTASE INHIBITORS+PFT/CT
L52          57 SEA FILE=MEDLINE ABB=ON  PLU=ON  L44 AND L51
L53           8 SEA FILE=MEDLINE ABB=ON  PLU=ON  L52 AND REVIEW/DT
```

HMG-CoA "

```
=> d que l54
L44      163056 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+PFT/CT
L48        8521 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYCLOOXYGENASE INHIBITORS+PFT/
                CT
L49         292 SEA FILE=MEDLINE ABB=ON  PLU=ON  L48 AND L44
L51        4556 SEA FILE=MEDLINE ABB=ON  PLU=ON  HYDROXYMETHYLGLUTARYL-COA
                REDUCTASE INHIBITORS+PFT/CT
L52          57 SEA FILE=MEDLINE ABB=ON  PLU=ON  L44 AND L51
L54           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L49 AND L52
```

Cox-2 inhib + HMG-CoA combo

```
=> s l50 or l53 or l54
L73          86 L50 OR L53 OR L54

=> dup rem l73 l72
FILE 'MEDLINE' ENTERED AT 16:24:57 ON 11 FEB 2004

FILE 'HCAPLUS' ENTERED AT 16:24:57 ON 11 FEB 2004
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PROCESSING COMPLETED FOR L72
L74          135 DUP REM L73 L72 (4 DUPLICATES REMOVED)
                ANSWERS '1-86' FROM FILE MEDLINE
                ANSWERS '87-135' FROM FILE HCAPLUS

=> d l74 bib ab 1-135

L74  ANSWER 1 OF 135     MEDLINE on STN                DUPLICATE 1
AN   2003030844     MEDLINE
DN   22425835   PubMed ID: 12538446
TI   The statins as anticancer agents.
AU   Chan Kelvin K W; Oza Amit M; Siu Lillian L
CS   Department of Medical Oncology and Hematology, Princess Margaret Hospital,
     University Health Network, Toronto, Ontario, M5G 2M9 Canada.
SO   CLINICAL CANCER RESEARCH, (2003 Jan) 9 (1) 10-9.  Ref: 98
     Journal code: 9502500. ISSN: 1078-0432.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
       General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA   English
FS   Priority Journals
EM   200307
ED   Entered STN: 20030123
     Last Updated on STN: 20030718
     Entered Medline: 20030717
AB   3-Hydroxy-3-methylgutaryl CoA reductase inhibitors, commonly referred to
     as the statins, have proven therapeutic and preventative effects in
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cardiovascular diseases. Recently, there are emerging interests in their use as anticancer agents based on preclinical evidence of their antiproliferative, proapoptotic, anti-invasive, and radiosensitizing properties. Inhibition of 3-hydroxy-3-methylgutaryl CoA reductase by the statins interferes with the rate-limiting step of the mevalonate pathway, leading to reduced levels of mevalonate and its downstream products, many of which play important roles in critical cellular functions such as membrane integrity, cell signaling, protein synthesis, and cell cycle progression. Perturbations of these processes in neoplastic cells by the statins may therefore result in control of tumor initiation, growth, and metastasis. The statins have demonstrated growth inhibitory activity in cancer cell lines and preclinical tumor models in animals. Phase I trials of statins in humans have demonstrated myotoxicity as their main dose-limiting toxicity, and Phase II trials in various tumor types are ongoing to evaluate their efficacy. Potential future directions in the development of the statins as anticancer agents include combinations with chemotherapeutic or other molecular-targeted agents, combinations with radiotherapy, maintenance therapy in minimal disease status, and as chemopreventive therapy.

L74 ANSWER 2 OF 135 MEDLINE on STN DUPLICATE 2
AN 2002613301 MEDLINE
DN 22257368 PubMed ID: 12369871
TI Selective cyclooxygenase-2 inhibitors and non-small cell lung cancer.
AU Gridelli C; Maione P; Airoma G; Rossi A
CS Division of Medical Oncology, S.G. Moscati Hospital, Avellino, Italy.. cgridelli@sirio-oncology.it
SO CURRENT MEDICINAL CHEMISTRY, (2002 Nov) 9 (21) 1851-8. Ref: 78
Journal code: 9440157. ISSN: 0929-8673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20021010
Last Updated on STN: 20030304
Entered Medline: 20030303
AB Lung cancer is the leading cause of death from cancer in most developed nations. The most common type of lung cancer is of non-small cell histology, representing approximately 80% of the total. Despite aggressive treatments in early stages and improvement of polychemotherapy outcomes in advanced disease, the five years survival rate for lung cancer remains under 15%. Fortunately, our improved knowledge of tumor biology and mechanisms of oncogenesis suggests several new potential targets for clinical research in cancer therapy. A substantial body of evidence indicates that cyclooxigenase (COX)-2 and prostaglandins (PGs) play an important role in tumorigenesis. Mechanisms involved in COX-2 participation in tumorigenesis and tumor growth include xenobiotic metabolism, angiogenesis stimulation, inhibition of immune surveillance and inhibition of apoptosis. COX-2 is frequently overexpressed in bronchial premalignancy, lung adenocarcinoma and squamous cell carcinoma and COX-2 overexpression is a marker of poor prognosis in surgically resected stage I non-small cell lung cancer. Treatment with COX-2 inhibitors reduces the growth of NSCLC cells in vitro and in xenograft studies. Recent studies have defined some of the mechanisms involved in

COX-2 participation in NSCLC development and diffusion. These evidences support the hypothesis that selective COX-2 inhibitors (coxibs) may prove beneficial in the prevention and treatment of NSCLC.

L74 ANSWER 3 OF 135 MEDLINE on STN DUPLICATE 3
AN 2002211807 MEDLINE
DN 21942476 PubMed ID: 11945149
TI COX selectivity and animal models for colon cancer.
AU Oshima Masanobu; Taketo Makoto M
CS Department of Pharmacology, Kyoto University Graduate School of Medicine, Yoshida-Kono cho, Sakyo-ku, Kyoto, 606-8501, Japan.
SO CURRENT PHARMACEUTICAL DESIGN, (2002) 8 (12) 1021-34. Ref: 160
Journal code: 9602487. ISSN: 1381-6128.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200208
ED Entered STN: 20020412
Last Updated on STN: 20020827
Entered Medline: 20020826
AB Early experiments performed during 1980s and 1990s using carcinogen-induced rat intestinal tumor models demonstrated the inhibitory effects of non-steroidal anti-inflammatory drugs (NSAIDs) on intestinal tumorigenesis. Furthermore, epidemiological studies and clinical trials for familial adenomatous polyposis (FAP) patients supported the possibility that NSAIDs can be used as chemopreventive agents. The major target molecules of NSAIDs are cyclooxygenases (COX), which catalyze the rate-limiting step of prostaglandin biosynthesis. Two isoenzymes of COX have been identified; COX-1 and COX-2. Whereas COX-1 is expressed constitutively in most tissues and responsible for tissue homeostasis, COX-2 is inducible and plays an important role in inflammation and intestinal tumorigenesis. A genetic study using compound mutant mice of COX-2(-)/(-), and Apc(Delta716) which is a model for human familial adenomatous polyposis (FAP), directly demonstrated that induction of COX-2 is critical for intestinal polyp formation. Numerous studies have also demonstrated that COX-2 selective inhibitors suppress intestinal polyp formation in Apc gene-mutant mice, and xenografted cancer cell growths. In addition, stimulation of angiogenesis is one of the major effects by COX-2 expression that is induced in the polyp stromal cells. On the other hand, another study indicated that COX-1 also plays an important role in the early stage of intestinal tumorigenesis. These data from animal model studies should be helpful in understanding the in vivo mechanism(s) of tumor suppression by NSAIDs or COX-2 inhibitors. Here, we review the animal studies that have been published as of August 2001, and reported to suppress intestinal tumor growths by NSAIDs or COX-2 inhibitors.

L74 ANSWER 4 OF 135 MEDLINE on STN DUPLICATE 4
AN 2002222188 MEDLINE
DN 21956893 PubMed ID: 11960327
TI HMG-CoA reductase inhibitors and the malignant cell: the statin family of drugs as triggers of tumor-specific apoptosis.
AU Wong W W L; Dimitroulakos J; Minden M D; Penn L Z
CS Department of Cellular and Molecular Biology, Ontario Cancer Institute, Princess Margaret Hospital, University Health Network, Toronto, Canada.

SO LEUKEMIA, (2002 Apr) 16 (4) 508-19. Ref: 170
Journal code: 8704895. ISSN: 0887-6924.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020418
Last Updated on STN: 20020508
Entered Medline: 20020507
AB The statin family of drugs target HMG-CoA reductase, the rate-limiting enzyme of the mevalonate pathway, and have been used successfully in the treatment of hypercholesterolemia for the past 15 years. Experimental evidence suggests this key biochemical pathway holds an important role in the carcinogenic process. Moreover, statin administration in vivo can provide an oncoprotective effect. Indeed, in vitro studies have shown the statins can trigger cells of certain tumor types, such as acute myelogenous leukemia, to undergo apoptosis in a sensitive and specific manner. Mechanistic studies show bcl-2 expression is down-regulated in transformed cells undergoing apoptosis in response to statin exposure. In addition, the apoptotic response is in part due to the depletion of the downstream product geranylgeranyl pyrophosphate, but not farnesyl pyrophosphate or other products of the mevalonate pathway including cholesterol. Clinically, preliminary phase I clinical trials have shown the achievable plasma concentration corresponds to the dose range that can trigger apoptosis of tumor types in vitro. Moreover, little toxicity was evident in vivo even at high concentrations. Clearly, additional clinical trials are warranted to further assess the safety and efficacy of statins as novel and immediately available anti-cancer agents. In this article, the experimental evidence supporting a role for the statin family of drugs to this new application will be reviewed.

L74 ANSWER 5 OF 135 MEDLINE on STN
AN 2003250700 MEDLINE
DN 22656373 PubMed ID: 12771797
TI Cyclooxygenase-2 as a potential target in the prevention and treatment of genitourinary tumors: a review.
AU Pruthi Raj S; Derksen Eric; Gaston Kris
CS Division of Urologic Surgery, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.
SO JOURNAL OF UROLOGY, (2003 Jun) 169 (6) 2352-9. Ref: 70
Journal code: 0376374. ISSN: 0022-5347.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200306
ED Entered STN: 20030531
Last Updated on STN: 20030611
Entered Medline: 20030610
AB PURPOSE: Recent years have seen a dramatic expansion in our discovery and knowledge of the molecular mechanisms of cancer development and progression. The discovery and elucidation of prostaglandin pathways, in

particular the molecular and clinical role of cyclooxygenase (COX)-2 function, has had important application to neoplasms. Current understanding of the role of COX-2 activity and, thereby, the potential clinical usefulness of COX-2 specific inhibitors as they apply to urological oncology are discussed. MATERIALS AND METHODS: The discovery of prostaglandin pathways, the molecular and clinical role of COX-2 function, and the corresponding application to neoplasms were reviewed in the scientific literature (MEDLINE from 1960 to the present). In particular, a thorough review of the current literature and recent abstract presentations at scientific meetings was done regarding the potential role of COX-2 in urological cancers (MEDLINE from 1960 to the present, and American Urological Association and American Society of Clinical Oncology annual meeting abstracts from1998 to the present). RESULTS: Decreased apoptosis, increased angiogenesis and immunosuppression are just some of the known sequelae of COX-2 over expression and each effect may have an important role in tumor formation and progression. Preclinical research and pilot clinical studies in urological oncology, in particular prostate, bladder and kidney cancer, have proved to be quite promising to date. CONCLUSIONS: Currently we are just beginning to understand the molecular mechanisms and clinical effects of COX-2 function and inhibition, and the potential for COX-2 specific inhibitors to affect potentially tumor biology and growth and, thereby, serve as antitumor drugs with therapeutic and chemopreventive roles for urological cancers. The absence of complete scientific understanding in these areas provides a generous opportunity for innovative and important scientific study.

L74 ANSWER 6 OF 135 MEDLINE on STN
AN 2003269842 MEDLINE
DN PubMed ID: 12796357
TI Tumor response to ionizing radiation combined with antiangiogenesis or vascular targeting agents: exploring mechanisms of interaction.
AU Wachsberger Phyllis; Burd Randy; Dicker Adam P
CS Division of Experimental Radiation Oncology, Department of Radiation Oncology, Kimmel Cancer Center, Jefferson Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.. phyllis.wachsberger@mail.tju.edu
NC P30CA56036-03 (NCI)
SO Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 Jun) 9 (6) 1957-71. Ref: 137
Journal code: 9502500. ISSN: 1078-0432.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030611
Last Updated on STN: 20040107
Entered Medline: 20040106
AB Recent preclinical studies have suggested that radiotherapy in combination with antiangiogenic/vasculature targeting agents enhances the therapeutic ratio of ionizing radiation alone. Because radiotherapy is one of the most widely used treatments for cancer, it is important to understand how best to use these two modalities to aid in the design of rational patient protocols. The mechanisms of interaction between antiangiogenic/vasculature targeting agents and ionizing radiation are

complex and involve interactions between the tumor stroma and vasculature and the tumor cells themselves. Vascular targeting agents are aimed specifically at the existing tumor vasculature. Antiangiogenic agents target angiogenesis or the new growth of tumor vessels. These agents can decrease overall tumor resistance to radiation by affecting both tumor cells and tumor vasculature, thereby breaking the codependent cycle of tumor growth and angiogenesis. The hypoxic microenvironment of the tumor also contributes to the mechanisms of interactions between antiangiogenic/vasculature targeting agents and ionizing radiation. Hypoxia stimulates up-regulation of angiogenic and tumor cell survival factors, giving rise to tumor proliferation, radioresistance, and angiogenesis. Preclinical evidence suggests that antiangiogenic agents reduce tumor hypoxia and provides a rationale for combining these agents with ionizing radiation. Optimal scheduling of combined treatment with these agents and ionizing radiation will ultimately depend on understanding how tumor oxygenation changes as tumors regress and regrow during exposure to these agents. This review article explores the complex interactions between antiangiogenic/vasculature targeting agents and radiation and offers insight into the mechanisms of interaction that may be responsible for improved tumor response to radiation.

L74 ANSWER 7 OF 135 MEDLINE on STN
AN 2003294523 MEDLINE
DN 22706246 PubMed ID: 12822012
TI [Chemoprevention of oral cancer].
Kjemoprevensjon av munnhulekreft.
AU Sudbo Jon
CS Det norske radiumhospital, Avdeling for onkologi, Fagomrade straleterapi, 0310 Oslo.. jon.sudbo@rh.uio.no
SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, (2003 May 29) 123 (11) 1518-21.
Ref: 22
Journal code: 0413423. ISSN: 0807-7096.
CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Norwegian
FS Priority Journals
EM 200311
ED Entered STN: 20030625
Last Updated on STN: 20031107
Entered Medline: 20031106
AB BACKGROUND: Morbidity and mortality from oral cancer is still considerable, and has not improved significantly over the last four or five decades. Early preventive intervention in persons at high risk may improve treatment results. MATERIAL AND METHODS: This review is based on our previously published data and by searches in the Medline and PubMed databases, using the following terms as key words: "oral premalignancies", "oral leukoplakia", "tumour progression", "genomic instability", "aneuploidy", "prognosis", "head and neck cancer", and "chemoprevention". RESULTS: Chemoprevention requires the early and reliable identification of persons at high risk of cancer. Retinoids have a clinically documented effect towards head-and-neck cancer, but are associated with unacceptable side-effects. Coxibs and inhibitors of epidermal growth factor receptors are candidate agents for chemoprevention of oral cancer. INTERPRETATION: It is now possible to identify persons at high risk of developing oral cancer who may benefit from chemopreventive use of coxibs or inhibitors of

epidermal growth factor receptors.

L74 ANSWER 8 OF 135 MEDLINE on STN
AN 2003294522 MEDLINE
DN 22706245 PubMed ID: 12822011
TI [Chemoprevention: treatment of persons at high risk of cancer]. Kjemoprevensjon--primaerforebyggende behandling ved hoy kreftrisiko.
AU Sudbo Jon
CS Avdeling for onkologi, Fagomradet straleterapi, Radiumhospitalet, 0310 Oslo.. jon.sudbo@rh.uio.no
SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, (2003 May 29) 123 (11) 1514-7. Ref: 33
Journal code: 0413423. ISSN: 0807-7096.
CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Norwegian
FS Priority Journals
EM 200311
ED Entered STN: 20030625
Last Updated on STN: 20031107
Entered Medline: 20031106
AB BACKGROUND: Solid malignant tumours are still associated with high mortality and morbidity. Chemoprevention--long-term systemic therapy in order to revert, stop or at least delay the carcinogenic process--is a feasible therapeutic approach to persons at increased risk of cancer. METHODS: References for this review article were identified by a search of Medline and PubMed for the years 1990 to 2002; the keywords used were "chemoprevention", "tamoxifen", "COX-2 inhibitors", "NSAIDs", "SERM", "EGFR", "breast cancer", "familial adenomatous polyposis coli", "colorectal cancer", "lung cancer", and "prostate cancer". RESULTS: Long-term medical treatment of persons at high-risk of cancer may reduce the incidence of several types of malignancies. This approach requires early and reliable identification of persons at high risk. INTERPRETATION: Chemoprevention is likely to become important in the future treatment of breast cancer, colorectal cancer, lung cancer, prostate cancer and probably also other malignancies. In order to ensure treatment effect and to avoid unnecessary side effects, such treatment should be restricted to persons at high risk.

L74 ANSWER 9 OF 135 MEDLINE on STN
AN 2003323579 MEDLINE
DN PubMed ID: 12854100
TI The prevention of breast cancer.
AU Prichard R S; Hill A D K; Dijkstra B; McDermott E W; O'Higgins N J
CS Surgical Professorial Unit, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland.
SO British journal of surgery, (2003 Jul) 90 (7) 772-83. Ref: 121
Journal code: 0372553. ISSN: 0007-1323.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200311

ED Entered STN: 20030711
Last Updated on STN: 20031218
Entered Medline: 20031117

AB BACKGROUND: Despite advances in the early detection and treatment of breast carcinoma, the mortality and morbidity rates associated with this disease remain high. Primary prevention, therefore, offers the best chance of making a major impact on outcome. METHODS: The aim was to review the rationale, current stage of development and adverse effects of the strategies involved in the primary prevention of breast carcinoma. A review of the literature was undertaken by searching the MEDLINE database for the period 1966-2002 without language restrictions. RESULTS AND CONCLUSION: Currently, the only agent to have general approval for chemoprevention of breast carcinoma is tamoxifen. Women who derive the greatest benefit in terms of risk reduction from tamoxifen are premenopausal with a 5-year Gail risk factor of more than 1.66 per cent, postmenopausal with a 5-year Gail risk factor of more than 3 per cent, and postmenopausal without a uterus. In these specific subgroups, tamoxifen should be considered for the chemoprevention of breast carcinoma. Raloxifene, retinoids, aromatase inhibitors and cyclo-oxygenase 2 inhibitors require further clinical investigation before adoption in this context. Surgical intervention should largely be limited to those women who have a BRCA1 or BRCA2 mutation.

L74 ANSWER 10 OF 135 MEDLINE on STN
AN 2003374785 MEDLINE
DN 22791105 PubMed ID: 12910508
TI Hepatocellular carcinoma: is there a potential for chemoprevention using cyclooxygenase-2 inhibitors?.
AU Koga Hironori
CS Second Department of Medicine, and Kurume University Research Center for Innovative Cancer Therapy, Kurume University, Kurume, Japan.. hirokoga@med.kurume-u.ac.jp
SO CANCER, (2003 Aug 15) 98 (4) 661-7. Ref: 110
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200308
ED Entered STN: 20030812
Last Updated on STN: 20030830
Entered Medline: 20030829

AB Inhibitors of cyclooxygenase-2 (COX-2) have proapoptotic and antiangiogenic effects on malignant tumors and inhibit their invasion to surrounding tissues. These properties are derived from COX-dependent and/or COX-independent signaling via peroxisome proliferator-activated receptor gamma. Although the role of COX-2 involvement in human hepatocarcinogenesis has not been determined yet, selective COX-2 inhibitors with COX-independent properties may potentially suppress hepatocarcinogenesis. This hypothesis should be confirmed in in vivo studies using animal models. These studies may provide insights into any application of the COX-2 inhibitor for primary and/or secondary chemoprevention.

L74 ANSWER 11 OF 135 MEDLINE on STN
AN 2003477913 MEDLINE
DN 22917798 PubMed ID: 14554238
TI Inhibitors of cyclo-oxygenase 2: a new class of anticancer agents?.
AU Gasparini Giampietro; Longo Raffaele; Sarmiento Roberta; Morabito Alessandro
CS Division of Medical Oncology, S Filippo Neri Hospital, Rome, Italy.. gasparini.oncology@tisclinet.it
SO Lancet Oncol, (2003 Oct) 4 (10) 605-15. Ref: 82
Journal code: 100957246. ISSN: 1470-2045.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20031015
Last Updated on STN: 20031028
Entered Medline: 20031027
AB Experimental studies have shown that cyclo-oxygenase 2 (COX2) is involved in tumour development and progression. Selective inhibitors of COX2 (coxibs) block tumour growth through many mechanisms, especially by antiangiogenic and proapoptotic effects. In experimental models, coxibs potentiate the activity of cytotoxic agents, hormones, and radiotherapy. Large clinical studies have shown chemopreventive activity of coxibs in colorectal cancer. The findings of preclinical studies coupled with the overexpression of COX2 observed in advanced human tumours are the basis for new therapeutic anticancer strategies based on combinations of coxibs with other anticancer treatment modalities. Early clinical studies have documented the feasibility, good tolerability, and promising activity of coxibs combined with chemotherapy in patients with advanced colorectal and non-small-cell lung cancers. Here, we describe the recent findings on the antitumour effects of coxibs with particular focus on the opportunities that have emerged for treatment of cancer.

L74 ANSWER 12 OF 135 MEDLINE on STN
AN 2003403530 MEDLINE
DN 22823084 PubMed ID: 12941579
TI New and emerging treatment options for multiple sclerosis.
AU Polman Chris H; Uitdehaag Bernard M J
CS Department of Neurology, VU Medical Center, Amsterdam, Netherlands.. ch.polman@vumc.nl
SO Lancet Neurol, (2003 Sep) 2 (9) 563-6. Ref: 31
Journal code: 101139309. ISSN: 1474-4465.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030828
Last Updated on STN: 20031024
Entered Medline: 20031023

AB BACKGROUND: The use of interferon beta and glatiramer acetate for the treatment of multiple sclerosis (MS) has, to some extent, changed the course of the disease. The annual relapse rate of patients treated with these drugs is lower than that in placebo-treated patients, and more treated patients remain relapse-free compared with untreated patients. In addition, these compounds reduce the development of new lesions, as detected by MRI. RECENT DEVELOPMENTS: The limited effectiveness of approved treatments for MS, as well as reports of adverse events and toxicity, emphasise the need for the development of new therapies with improved efficacy and fewer side-effects. Clinical observations, increased understanding of the underlying pathophysiology of the disease, and advances in biotechnology have led to several new therapeutic approaches to the treatment of MS that are currently under investigation. WHERE NEXT? Mitoxantrone has recently been shown to produce benefit when used to treat patients with progressive MS; it may also be an effective second-line treatment for patients who do not respond to interferon beta or glatiramer acetate. Over the past few years, several studies have drawn attention to the potential of natalizumab, alemtuzumab, statins, and oestrogens as effective treatments for MS. These drugs are at different stages of clinical development and additional clinical data are needed to support their use and devise dosage regimens. However, they are important and attractive candidates for several reasons: they counteract a fundamental and well-defined pathophysiological process; they have a less cumbersome route of administration than interferon beta and glatiramer acetate; or they have a remarkable safety record.

L74 ANSWER 13 OF 135 MEDLINE on STN
AN 2003368144 MEDLINE
DN PubMed ID: 12901943
TI Cyclooxygenase inhibitors: drugs for cancer prevention.
AU Shiff Steven J; Shivaprasad Punitha; Santini Diana L
CS Diet and Nutrition in the Prevention of Chronic Diseases, Cancer Institute of New Jersey, University of Medicine & Dentistry of NJ/Johnson Medical School, 195 Little Albany Street, New Brunswick, NJ 08903, USA.. shiffst@umdnj.edu
NC P30 CA 72720 (NCI)
R01 CA 73298 (NCI)
SO Current opinion in pharmacology, (2003 Aug) 3 (4) 352-61. Ref: 76
Journal code: 100966133. ISSN: 1471-4892.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040107
Entered Medline: 20040106
AB Evidence that chronic intake of non-steroidal anti-inflammatory drugs, especially aspirin, prevents cancer development continues to accumulate. The data are particularly convincing for colorectal cancer; however, because of well-known side effects, they cannot routinely be recommended for this purpose. An appreciation of the mechanisms that underlie their anti-cancer effects might permit the development of safer agents. Intensive investigation has led to the characterization of several potential chemopreventive mechanisms of action of these drugs.

Antineoplastic actions could result from effects on overlapping processes in the different cell-types that comprise tumors, such as epithelial and stromal cells.

L74 ANSWER 14 OF 135 MEDLINE on STN
AN 2003387719 MEDLINE
DN 22805669 PubMed ID: 12924030
TI [Statins in the treatment of tumors. Fiction or a new therapeutic approach?].
Statiny v lecbe nadorovych onemocneni. Fikce nebo novy terapeuticky pristup?.
AU Vitek L; Kraslova I; Muchova L; Krechler T
CS IV. interni klinika 1, Ustav klinicke biochemie a laboratorni diagnostiky 1. LF UK a VFN, Praha.. vitek@cesnet.cz
SO CASOPIS LEKARU CESKYCH, (2003) 142 (6) 323-8; discussion 329-30. Ref: 80
Journal code: 0004743. ISSN: 0008-7335.
CY Czech Republic
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Czech
FS Priority Journals
EM 200310
ED Entered STN: 20030820
Last Updated on STN: 20031010
Entered Medline: 20031009
AB HMG-CoA reductase inhibitors (statins) belong to the key hypocholesterolemic drugs. Besides this very important function, several others have been recently demonstrated such as the inhibition of atherogenous plaque formation, platelet aggregation, or improvement of endothelial function and fibrinolytic activity, or even the direct protective effects of statins on the mortality of acute myocardial infarction. Aside from the major interest of both the medical community and pharmaceutical companies remain the very important anti-tumor effects of this group of drugs. As based on recent medical research, inhibition of HMG-CoA reductase, the key enzyme in the cholesterol biosynthesis, brings about depletion of several intermediates. The most important one seems to be farnesyl pyrophosphate, which has a very important role in the cell signaling affecting apoptosis. The aim of the survey is to summarize present knowledge in this medical field and to demonstrate the enormous curative potential of this group of drugs.

L74 ANSWER 15 OF 135 MEDLINE on STN
AN 2003390328 MEDLINE
DN 22808321 PubMed ID: 12927571
TI Activity of the non-steroidal anti-inflammatory drug indomethacin against colorectal cancer.
AU Hull M A; Gardner S H; Hawcroft G
CS Molecular Medicine Unit, University of Leeds, Clinical Sciences Building, St. James's University Hospital, Leeds, LS9 7TF, UK.. M.A.Hull@leeds.ac.uk
SO CANCER TREATMENT REVIEWS, (2003 Aug) 29 (4) 309-20. Ref: 123
Journal code: 7502030. ISSN: 0305-7372.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 200309
ED Entered STN: 20030821
Last Updated on STN: 20030924
Entered Medline: 20030923
AB A substantial body of evidence from rodent colon carcinogenesis models, in vitro experiments with human colorectal cancer cells and limited clinical observations in humans suggest that the non-steroidal anti-inflammatory drug indomethacin has anti-colorectal cancer activity. However, although many mechanisms of the anti-neoplastic activity of indomethacin have been suggested, e.g., cyclooxygenase inhibition and peroxisome proliferator-activated receptor gamma activation, the precise relevance of the majority of in vitro pharmacological observations to the in vivo anti-neoplastic activity of indomethacin remains unclear. Herein, we review the existing literature describing the chemopreventative and chemotherapeutic efficacy of indomethacin against colorectal cancer, and draw together the disparate literature describing potential mechanisms of action of indomethacin in human colorectal cancer cells in vitro. Although indomethacin itself has significant adverse effects, including serious upper gastrointestinal toxicity, the development of novel derivatives that may have an improved safety profile means that further investigation of the anti-colorectal cancer activity of indomethacin is warranted.

L74 ANSWER 16 OF 135 MEDLINE on STN
AN 2003445860 MEDLINE
DN PubMed ID: 14506383
TI Cyclo-oxygenase inhibition in colorectal adenomas and cancer.
AU Ricchi Paolo; Pignata Sandro; Iaffaioli Rosario Vincenzo; Daniele Bruno
CS Department of Biologia e Patologia cellulare e molecolare "L. Califano", Centro di Endocrinologia ed Oncologia Sperimentale "G. Salvatore" del Consiglio Nazionale delle Ricerche, Universita "Federico II", Napoli, Itali.
SO Journal of clinical gastroenterology, (2003 Oct) 37 (4) 281-7. Ref: 70
Journal code: 7910017. ISSN: 0192-0790.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200402
ED Entered STN: 20030925
Last Updated on STN: 20040210
Entered Medline: 20040209
AB Increasing evidence indicates that Non-steroidal anti-inflammatory drugs (NSAIDs), compounds that inhibit the enzymatic activity of cyclooxygenase (COX), can reduce the number and size of adenomas in patients with familial adenomatous polyposis as well as the incidence of colorectal cancer. The COX enzyme family consists of the classic COX-1 and a second enzyme, COX-2, which is induced by various stimuli, such as mitogens and cytokines. While it is well proven that COX-2 overexpression is a central event in colorectal carcinogenesis, that prostaglandins (PGs) can contribute to tumorigenesis, and that COX-2 selective inhibitors are active chemopreventive agents, the molecular mechanisms by which NSAIDs exert their chemopreventive effect is not fully understood. However, significant advances have been made in understanding the interference of

NSAIDs with the pathways that control cell growth and survival even independently from their COX-inhibiting properties, making their use attractive both alone and in combination with standard therapies in the treatment of advanced colorectal cancer. In addition, the recently recognized anti-angiogenic and radiosensitizer properties of COX-2 inhibitors support, further suggest their use in the adjuvant setting.

L74 ANSWER 17 OF 135 MEDLINE on STN
AN 2003269261 MEDLINE
DN 22680115 PubMed ID: 12795058
TI Chemotherapy with cyclooxygenase-2 inhibitors in the treatment of malignant disease: pre-clinical rationale and preliminary results of clinical trials.
AU Blanke Charles D; Masferrer Jaime L
CS Oregon Health & Science University, Portland, Oreg., USA.. blankec@ohsu.edu
SO PROGRESS IN EXPERIMENTAL TUMOR RESEARCH, (2003) 37 243-60. Ref: 62
Journal code: 0376446. ISSN: 0079-6263.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200308
ED Entered STN: 20030611
Last Updated on STN: 20030815
Entered Medline: 20030814

L74 ANSWER 18 OF 135 MEDLINE on STN
AN 2003269259 MEDLINE
DN 22680113 PubMed ID: 12795056
TI Potential for combined modality therapy of cyclooxygenase inhibitors and radiation.
AU Saha Debabrata; Choy Hak
CS Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, Tenn., USA.
SO PROGRESS IN EXPERIMENTAL TUMOR RESEARCH, (2003) 37 193-209. Ref: 49
Journal code: 0376446. ISSN: 0079-6263.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200308
ED Entered STN: 20030611
Last Updated on STN: 20030815
Entered Medline: 20030814
AB In conclusion, COX-2 inhibitors have potent anti-tumorigenic activity. Results from animal studies strongly indicate that the likely mechanism for enhanced TGD and TCD50 in tumors treated with radiation and COX-2 inhibitors was the inhibition of angiogenesis. In our recent findings we observed that the antagonists of angiogenesis also inhibited the endogenous as well as phorbol-ester-mediated induction of COX-2 expression in human lung cancer cell lines and that in the xenograft model a combination of angiogenic antagonists and radiation significantly delayed

tumor growth [ASCO 2002, Vol. 21 (Part 1); p445a, #1779]. In human tumor models, apoptosis was another mechanism of cell death. Furthermore, it was demonstrated that COX-2 inhibitors could change the intrinsic radiosensitivity of human cancer cells [41]. Therefore, inhibition of angiogenesis by COX-2 inhibitors may be the major mechanism for increased radiation effects in tumors. However, other mechanisms such as changes in tumor perfusion, apoptosis, and an increase in intrinsic radiation sensitivity must also be considered. Inhibitors of COX-2 in combination with radiation therapy may be an alternative strategy that can be tested in clinical trials. The combination of COX-2 inhibitors and radiation suggest a complementary strategy to target angiogenesis while potentially minimizing the impact on quality of life. Currently, the Radiation Therapy Oncology Group [www.rtog.org] is just one of the National Cancer Institute sponsored cooperative groups conducting clinical trials in cervix cancer, lung cancer and brain tumors, using inhibitors of COX-2 in combination with chemotherapy and radiation therapy. These clinical trials will help elucidate the role of this interesting class of agents in combination with cytotoxic therapy for the treatment of cancer.

L74 ANSWER 19 OF 135 MEDLINE on STN
AN 2003116000 MEDLINE
DN 22516529 PubMed ID: 12628511
TI Mechanisms and applications of non-steroidal anti-inflammatory drugs in the chemoprevention of cancer.
AU Steele Vernon E; Hawk Ernest T; Viner Jaye L; Lubet Ronald A
CS Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892-7322, USA.. vsly@nih.gov
SO MUTATION RESEARCH, (2003 Feb-Mar) 523-524 137-44. Ref: 63
Journal code: 0400763. ISSN: 0027-5107.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030312
Last Updated on STN: 20030425
Entered Medline: 20030424
AB Biological and chemical irritants can be the cause of irritation in a variety of organ sites. It is becoming well understood that chronic irritation in any form can initiate and accelerate the cancer process in these same organs. This understanding comes in part from the many epidemiologic studies which point out that chronic inflammation correlates with increased risk of developing cancer in that organ which is affected. One of the hallmarks of chronic irritation is the increased activity in the arachidonic acid pathway which provides many of the necessary inflammatory biochemical mediators to this process. Arachidonic acid metabolism diverges down two main pathways, the cyclooxygenase (COX) and the lipoxygenase (LOX) pathways. The COX pathway leads to prostaglandin and thromboxane production and the LOX pathway leads to the leukotrienes (LTs) and hydroxyeicosatetraenoic acids (HETEs). These classes of inflammatory molecules exert profound biological effects which enhance the development and progression of human cancers. A large number of synthetic drugs and natural products have been discovered that block many of these key pathways. Much experimental evidence in animals has shown that

inhibition of the key enzymes which drive these pathways can, in fact, prevent, slow or reverse the cancer process. The data are convincing in a number of organ sites including colon, breast, lung, bladder and skin. More recently, double-blinded randomize clinical trials in humans have shown the prevention of colonic polyps by anti-inflammatory agents. These studies have primarily used non-steroidal anti-inflammatory drugs (NSAIDS) which block the COX pathways. Recent preclinical studies indicate that the LOX pathway also may be an important target for cancer prevention strategy. The expression of high levels of these enzymes in cancerous tissues make them an obvious first target for cancer prevention strategies. As newer more specific drugs are developed with few adverse effects this important prevention strategy may become a reality.

L74 ANSWER 20 OF 135 MEDLINE on STN
AN 2003224150 MEDLINE
DN 22630717 PubMed ID: 12745645
TI Cancer therapy: new targets for chemotherapy.
AU Novotny Ladislav; Szekeres Thomas
CS Kuwait Unviersity, Faculty of Parmacy, Department of Chemistry, Kuwait, Kuwait.. novotny@hsc.kuniv.edu.kw
SO Hematology, (2003 Jun) 8 (3) 129-37. Ref: 63
Journal code: 9708388. ISSN: 1024-5332.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200309
ED Entered STN: 20030515
Last Updated on STN: 20030903
Entered Medline: 20030902
AB The number two cause of mortality in developed countries is cancer. Despite the enormous effort put into cancer prevention, early diagnosis and treatment, it is likely that the incidence of the cancer morbidity and mortality will increase for the foreseeable future. This is due to various factors such as increased life expectancy, changes in environment and also the socio-economic situation around the world. Some cancer attracts more attention than others and increasingly epidemiological information is reaching the general public and is beginning to influence behavior. It is now well recognized that, for example, 1 of 8 women in the industrialized world will be diagnosed with breast cancer. Additionally, a strong correlation was established between lung cancer incidence and smoking and it is broadly accepted that the incidence of colon cancer is directly related to age and diet, and has been increasing over time. The current failure of preventive measures to significantly reduce the increasing incidence of these common tumors illustrates the importance of effective cancer treatment strategies, including chemotherapy. The combination of various anticancer drugs, given together with surgery and radiotherapy, gives hope to many patients. There has been recent evidence of improved therapeutic outcome with recent approaches and newer agents but for continuing effective chemotherapeutic treatment there is a need for a detailed understanding of their mechanisms of action and on the rationale of their application. This review attempts to provide up-to-date information regarding the development of new and innovative treatment strategies for cancer chemotherapy. Virtually, every year several of new targets for cancer therapy on both, cellular and

molecular levels, are identified and new drugs enter not only clinical trials but also are included in well accepted and documented therapeutic protocols. As this review is in addition to our review published previously (Medical Principles and Practice 11, 2002, 117-125), we have tried to include new and innovative targets and drugs that attract attention at present. Although it is not possible to provide a complete list of all achievements and cover all work done in this field, we hope to be able to give some insight into this rapidly developing area.

L74 ANSWER 21 OF 135 MEDLINE on STN
AN 2003105254 MEDLINE
DN 22505176 PubMed ID: 12618325
TI Cyclooxygenase-2 and prostate carcinogenesis.
AU Hussain Tajamul; Gupta Sanjay; Mukhtar Hasan
CS Department of Dermatology, University of Wisconsin, Medical Science Center, 1300 University Avenue, Madison, WI 53706, USA.
NC R03 CA 89739 (NCI)
SO CANCER LETTERS, (2003 Mar 10) 191 (2) 125-35. Ref: 82
Journal code: 7600053. ISSN: 0304-3835.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030306
Last Updated on STN: 20030502
Entered Medline: 20030501
AB In recent years a dramatic surge has occurred on studies defining to the role of cyclooxygenase (COX)-2 in causation and prevention of cancer. Prostaglandin (PG) endoperoxidase synthase also commonly referred to as COX is a key enzyme involved in the conversion of arachidonic acid to PGs and other eicosanoids. COX exists as two isoforms, namely COX-1 and COX-2 with distinct tissue distribution and physiological functions. COX-1 is constitutively expressed in many tissues and cell types and is involved in normal cellular physiological functions whereas COX-2 is pro-inflammatory in nature and is inducible by mitogens, cytokines, tumor promoters and growth factors. A large volume of data exists showing that COX-2 is overexpressed in a large number of human cancers and cancer cell lines. The possibility of COX-2 as a candidate player in cancer development and progression evolved from the epidemiological studies which suggest that regular use of aspirin or other non-steroidal anti-inflammatory drugs could significantly decrease the risk of developing cancers in experimental animals and in humans. In our recently published study (Prostate, 42 2000 73-78), we provided the first evidence that COX-2 is overexpressed in human prostate adenocarcinoma. Many other studies verified our initial observation and reported that compared to normal tissue, COX-2 is overexpressed in human prostate cancer. It should be noted that some recent work has suggested that COX-2 is only up-regulated in proliferative inflammatory atrophy of the prostate, but not in prostate carcinoma. In this scenario, COX-2 inhibitors could afford their effects against prostate carcinogenesis by modulating COX-2 activity in other cells in prostate. An exciting corollary to this ongoing work is that selective COX-2 inhibitors may exhibit chemopreventive and even chemotherapeutic effects against prostate carcinogenesis in humans.

L74 ANSWER 22 OF 135 MEDLINE on STN
AN 2003367817 MEDLINE
DN PubMed ID: 12902869
TI Why cyclooxygenase-2 inhibition plus chemotherapy?.
AU Sweeney Christopher J
CS Indiana University, Indianapolis, Indiana 46202, USA.. chsweene@iupui.edu
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S122-5. Ref: 42
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB New approaches to treating cancers are needed. Preclinical studies have identified numerous candidate genes/proteins that promote the cancer process. Cyclooxygenase-2 (COX-2) is a reasonable "target" because it is found in many epithelial tumors, has been shown to portend a poor prognosis, and is involved in many processes that promote cancer progression and chemotherapy resistance. Inhibition of COX-2 also has the potential to provide supportive care to patients with cancer. This article describes the rationale for performing a phase II trial of specific COX-2 inhibition in combination with chemotherapy to define toxicity and efficacy. However, as with most new therapies, phase III trials will be needed to determine whether specific COX-2 therapy is able to improve patient outcome with a reasonable safety profile.

L74 ANSWER 23 OF 135 MEDLINE on STN
AN 2003367815 MEDLINE
DN PubMed ID: 12902867
TI COX-2 inhibitors as radiation sensitizers for upper GI tract cancers: esophagus, stomach, and pancreas.
AU Rich Tyvin A; Shepard Robert
CS Department of Radiation Oncology, University of Virginia Health Sciences System, Charlottesville 22901, USA.. tar4d@virginia.edu
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S110-3. Ref: 33
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB Cancers of the esophagus, stomach, and pancreas have been successfully treated recently with combinations of radiosensitizing chemotherapy and irradiation. New approaches building onto 5-fluorouracil chemoradiation

include capecitabine (Xeloda) and irradiation. Capecitabine is an oral 5-fluorouracil (5-FU) prodrug that is more convenient than using infusional 5-FU, appears to have a similar therapeutic profile, and can be combined with daily irradiation. The addition of a cyclooxygenase-2 (COX-2) inhibitor is being investigated in upper gastrointestinal cancer sites because there is a high degree of overexpression of COX-2 in these cancers.

L74 ANSWER 24 OF 135 MEDLINE on STN
AN 2003115997 MEDLINE
DN 22516525 PubMed ID: 12628507
TI Chemoprevention of colon cancer by Korean food plant components.
AU Kim Dae Joong; Shin Dong Hwan; Ahn Byeongwoo; Kang Jin Seok; Nam Ki Taek; Park Cheol Beom; Kim Cheul Kyu; Hong Jin Tae; Kim Yun-Bae; Yun Young Won; Jang Dong Deuk; Yang Ki-Hwa
CS Structural BioInformatics & Cancer Prevention, College of Veterinary Medicine & Research Institute of Veterinary Medicine, Chungbuk National University, 48 Gaeshin-dong, Heungduk-gu, Cheongju 361-763, South Korea.. kimdj@cbu.ac.kr
SO MUTATION RESEARCH, (2003 Feb-Mar) 523-524 99-107. Ref: 50
Journal code: 0400763. ISSN: 0027-5107.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030312
Last Updated on STN: 20030425
Entered Medline: 20030424
AB Inducible cyclooxygenase (COX-2) and inducible nitric oxide synthase (iNOS/NOS-2) play pivotal roles as mediators of inflammation involved in early steps of carcinogenesis in certain organs. Therefore, chemoprevention is theoretically possible through inhibition of COX-2 and/or iNOS. In the present study, we examined the chemopreventive effects of indole-3-carbinol (I3C), a constituent of cruciferous vegetables (the family of Cruciferae) such as cabbages, cauliflowers and broccoli on the multiple intestinal neoplasia (Min) genetic mouse model, and on mouse colon carcinogenesis induced by azoxymethane (AOM). The consumption of cruciferous vegetables such as cabbage, broccoli, and Brussels sprouts has been shown to have cancer chemopreventive effects in humans and experimental animals. I3C has been shown to exert a cancer chemopreventive influence in liver, colon, and mammary tissue when given before or concurrent with exposure to a carcinogen. Powdered AIN-76A diets (Harlan Teklad Research Diet, Madison, USA) containing 100 or 300 ppm I3C (group 1 or 2) or the same pellet diets without supplement (group 3) were fed to 6-week-old male C57BL/6J-Apc(Min)(/+) (Min/+) mice (The Jackson Laboratory, Bar Harbor, ME, USA) for 10 weeks. In addition the same diets were given to wild-type normal C57BL/6J-Apc(Min)(/+) littermates after AOM initiation (groups 4-7: 10 mice in each group) for 32 weeks from week 4. At 16 weeks of age, all Min/+ mice (groups 1-3) were sacrificed for assessment of intestinal polyp development. The incidences of the colonic adenomatous polyps in the groups 1-3 were 60% (12/20), 60% (15/25) and 84% (21/25), respectively. A decreasing tendency in multiplicities of the colonic adenomatous polyps in group 1 (I3C 100 ppm; 0.85 +/- 0.22; 61%) and group 2 (I3C 300 ppm; 1.32 +/- 0.28; 94%) was

observed when compared with group 3 (control; 1.40 +/- 0.21; 100%). Total number of aberrant crypt foci (ACF)/colon or aberrant crypts (AC)/colon in wild-type mice of group 4 or 5 were decreased significantly compared with those of the AOM alone group (group 6) ($P < 0.01$). These results suggest that I3C may be a potential chemopreventive agent for colon cancer.

L74 ANSWER 25 OF 135 MEDLINE on STN
AN 2003367811 MEDLINE
DN PubMed ID: 12902863
TI Combination of a COX-2 inhibitor with radiotherapy or radiochemotherapy in the treatment of thoracic cancer.
AU Liao Zhongxing; Milas Luka; Komaki Ritsuko; Stevens Craig; Cox James D
CS Division of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.. zliao@mdanderson.org
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S85-91. Ref: 51
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB Cyclooxygenase-2 (COX-2) is an enzyme involved in prostaglandin production in pathologic states such as inflammatory processes and cancer. The enzyme is often overexpressed in premalignant lesions and cancer, including cancers of the lung and esophagus. Inhibition of this enzyme with selective COX-2 inhibitors was found to enhance tumor response to radiation in preclinical studies, suggesting that these agents can improve the response of various cancers to radiotherapy. On the basis of these preclinical findings, clinical trials of the combination of celecoxib, a selective COX-2 inhibitor, with radiotherapy were initiated in patients with lung carcinoma and with chemoradiotherapy in patients with esophageal carcinoma. The rationale for using selective COX-2 inhibitors is discussed, and the current clinical protocols and the initial findings are described.

L74 ANSWER 26 OF 135 MEDLINE on STN
AN 2003367810 MEDLINE
DN PubMed ID: 12902862
TI Initial experience combining cyclooxygenase-2 inhibition with chemoradiation for locally advanced pancreatic cancer.
AU Crane Christopher H; Mason Kathy; Janjan Nora A; Milas Luka
CS Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.. ccrane@mdanderson.org
NC CA06294 (NCI)
CA16672 (NCI)
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S81-4. Ref: 19
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB Pancreatic cancer is a lethal disease that is resistant to chemotherapy and radiotherapy. Gemcitabine has recently been shown to be an improvement over 5-fluorouracil in patients with advanced disease. It is also a potent radiosensitizer, which has led to the investigation of gemcitabine with concurrent radiotherapy. However, preliminary results indicate that there are significant limitations to this approach in this challenging disease. Pancreatic cancer cells have alterations in many molecular signaling pathways that may be responsible for their resistance to cytotoxic therapy and aggressive behavior. Cyclooxygenase-2 (COX-2) is commonly overexpressed in pancreatic tumors, and preclinical evidence indicates that selective COX-2 inhibition enhances both chemotherapy and radiotherapy response, without affecting normal tissue damage. We have initiated preclinical studies as well as a phase I clinical protocol evaluating the combination of gemcitabine and celecoxib (Celebrex) with radiotherapy. In preclinical studies, celecelecoxib strongly enhanced the antitumor efficacy of chemoradiation. However, preliminary observations from both the preclinical experiments as well as the clinical protocol have revealed more toxicity with this combination than with gemcitabine and radiotherapy alone. These observations require further study, but are cause for concern when combining gemcitabine, radiotherapy, and celecoxib.

L74 ANSWER 27 OF 135 MEDLINE on STN
AN 2003335537 MEDLINE
DN PubMed ID: 12867065
TI The importance of the eicosanoid pathway in lung cancer.
AU Laskin Janessa J; Sandler Alan B
CS Department of Medical Oncology and Hematology, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, 777 PRB, Nashville, TN 37215-6307, USA.
SO Lung cancer (Amsterdam, Netherlands), (2003 Aug) 41 Suppl 1 S73-9. Ref: 34
Journal code: 8800805. ISSN: 0169-5002.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200311
ED Entered STN: 20030718
Last Updated on STN: 20031218
Entered Medline: 20031118
AB Non-steroidal anti-inflammatory agents (NSAIDs) inhibit the conversion of arachadonic acid to a class of inflammatory mediators known as eicosanoids. These minimally toxic drugs have demonstrated important anti-cancer properties in colorectal cancer and pre-clinical models have shown their potential for use in the treatment of non-small cell lung cancer (NSCLC). Clinical trials are underway investigating the efficacy of eicosanoid inhibitors alone and in combination with radiation and

chemotherapy.

L74 ANSWER 28 OF 135 MEDLINE on STN
AN 2003167169 MEDLINE
DN 22571460 PubMed ID: 12684131
TI Challenges and opportunities to the design and implementation of chemoprevention trials for prostate cancer.
AU Thompson Ian M; Basler Joseph A; Leach Robin; Troyer Dean; Klein Eric; Brawley Otis
CS Division of Urology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.. thompsoni@uthscsa.edu
SO Urol Oncol, (2003 Jan-Feb) 21 (1) 73-8. Ref: 19
Journal code: 9805460. ISSN: 1078-1439.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030410
Last Updated on STN: 20031016
Entered Medline: 20031015
AB Since 1991 and the activation of the Prostate Cancer Prevention Trial as well as similar prevention studies in several other organ sites, the interest in prostate cancer prevention has increased substantially. Despite such interest, the challenges to prevention trials-in design, implementation, prioritization, and allocation of resources-are substantial. Simultaneously, there has been an explosion in new targets and agents that may have an effect in the prevention of this disease. In this manuscript, we discuss these challenges to the study of prostate cancer prevention and provide a blueprint for prioritization of future studies.

L74 ANSWER 29 OF 135 MEDLINE on STN
AN 2003367808 MEDLINE
DN PubMed ID: 12902860
TI COX-2 inhibitor as a radiation enhancer: new strategies for the treatment of lung cancer.
AU Saha Debabrata; Pyo Hongryull; Choy Hak
CS Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, Tennessee 37232-5671, USA.
NC CA82117-02 (NCI)
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S70-4. Ref: 33
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB Lung cancer is one of the most common causes of cancer-related mortality

throughout the world, and the incidence continues to increase. Smoking is the number one cause of lung cancer. Emerging data have implicated cyclooxygenase-2 (COX-2) and prostanoid production in the pathogenesis of lung carcinoma. In invasive lung tumors, COX-2 upregulation has been reported in up to 90% of cases. COX-2 upregulation is an early event in the development of non-small-cell lung cancer and may be integral to the development of new blood vessels and production of specific proteases that are critical to growth and spread of lung malignancies. COX-2 inhibitors are known to enhance the chemosensitivity in COX-2 overexpressing lung cancer cell lines. Recently, we have demonstrated that selective COX-2 inhibitors also enhance the effect of radiation in COX-2 overexpressed cells. Therefore, inhibitors of COX-2 in combination with chemoradiation therapy may be an alternative strategy that can be tested in clinical trials. The combination of COX-2 inhibitors and radiation suggest a complementary strategy to target angiogenesis while potentially minimizing the impact on quality of life. Currently, several groups are conducting clinical trials in cervix cancer, lung cancer, and brain tumors, using inhibitors of COX-2 in combination with chemotherapy and radiation therapy. These clinical trials will help to elucidate the role of this interesting class.

L74 ANSWER 30 OF 135 MEDLINE on STN
AN 2003367805 MEDLINE
DN PubMed ID: 12902857
TI COX-2 inhibitors as radiosensitizing agents for cancer therapy.
AU Davis Thomas W; Hunter Nancy; Trifan Ovidiu C; Milas Luka; Masferrer Jaime L
CS Pharmacia Corporation, St. Louis, Missouri, USA.
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S58-61. Ref: 30
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB Prostaglandins have long been known to impact the radiosensitivity of cells and tissues, and many studies have centered on exploiting nonspecific prostaglandin inhibitors such as NSAIDs for therapeutic gain. These studies have ultimately been unsuccessful due to the lack of targeted specificity against the tumor. The discovery of the inducible cyclooxygenase enzyme (COX-2) and development of some highly selective inhibitors (which spare the constitutive COX-1 activity) has renewed excitement for modulating tumor prostaglandins as a method of specific radiosensitization of tumors, while sparing normal tissues. This review discusses these new data and generates a rationale for use of COX-2 inhibitors as radiosensitizing agents in cancer therapy.

L74 ANSWER 31 OF 135 MEDLINE on STN
AN 2003367804 MEDLINE
DN PubMed ID: 12902856
TI Development of COX inhibitors in cancer prevention and therapy.

AU Umar Asad; Viner Jaye L; Anderson William F; Hawk Ernest T
CS Gastrointestinal & Other Cancers Research Group, National Cancer Institute, Division of Cancer Prevention, Bethesda, Maryland 20892-7317, USA.
SO American journal of clinical oncology : official publication of the American Radium Society, (2003 Aug) 26 (4) S48-57. Ref: 193
Journal code: 8207754. ISSN: 1537-453X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030807
Last Updated on STN: 20040129
Entered Medline: 20040128
AB On the strength of in vitro, in vivo, observational, and clinical data, nonsteroidal antiinflammatory drugs (NSAIDs)-also referred to as COX inhibitors-have emerged as lead compounds for cancer prevention, and possible adjuncts to cancer therapy. Thus far, the routine use of NSAIDs for these indications is limited, largely owing to toxicity concerns, the paucity of efficacy data for any specific target organ, and uncertainties with regard to the most appropriate regimen (i.e., the best agent, formulation, dose, route of administration, and duration). Strategies to address these concerns primarily aim to improve the therapeutic index (i.e., benefit:risk ratio) of COX inhibitors by 1) minimizing systemic exposures whenever feasible, 2) achieving greater mechanistic specificity, 3) coadministering agents that provide prophylaxis against common toxicities, and 4) coadministering other effective anticancer agents. Clinical trials testing most of these strategies have been completed or are under way. The National Cancer Institute has a substantial research portfolio dedicated to the identification, testing, and development of NSAIDs as preventive and therapeutic anticancer agents. Discovering how to apply NSAIDs in persons with-or at risk for-cancer, although challenging, has the potential for considerable clinical and public health benefits.

L74 ANSWER 32 OF 135 MEDLINE on STN
AN 2003354921 MEDLINE
DN 22769348 PubMed ID: 12886870
TI Irinotecan, cisplatin/carboplatin, and COX-2 inhibition in small-cell lung cancer.
AU Natale Ronald B
CS Cedars-Sinai Comprehensive Cancer Center, National Lung Cancer Research Program, Salick Health Care, Inc., 8700 Beverly Blvd, Suite C2000, Los Angeles, CA 90048-1804, USA.. rnatale@csccc.salick.com
SO ONCOLOGY, (2003 Jul) 17 (7 Suppl 7) 22-6. Ref: 13
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030731

Last Updated on STN: 20031024
Entered Medline: 20031023

AB Recent findings indicate significant prolongation of survival and time to disease progression with irinotecan (CPT-11, Camptosar)/cisplatin vs etoposide/cisplatin in extensive-stage small-cell lung cancer, and a larger-scale phase III trial has been planned to provide more definitive data on the benefits of the irinotecan/cisplatin combination in this setting. Early-phase studies indicate that the activity of carboplatin (Paraplatin) in small-cell lung cancer is comparable to that of cisplatin, and that combining irinotecan on a day 1 and 8 schedule with split-dose carboplatin is feasible. Inhibition of the cyclooxygenase-2 (COX-2) enzyme, which is active in tumorigenesis, may augment efficacy and reduce toxicity of platinum/irinotecan combinations. A phase II trial has been designed to compare irinotecan/carboplatin and irinotecan/cisplatin combinations with or without the COX-2 inhibitor celecoxib (Celebrex) in patients with extensive-stage small-cell lung cancer. Results of these trials will help define the roles of platinum/irinotecan combinations and COX-2 inhibition in treatment for small-cell lung cancer.

L74 ANSWER 33 OF 135 MEDLINE on STN
AN 2003274572 MEDLINE
DN 22685780 PubMed ID: 12800601
TI Improvement of radiotherapy or chemoradiotherapy by targeting COX-2 enzyme.
AU Milas Luka; Mason Kathryn A; Crane Christopher H; Liao Zhongxing; Masferrer Jaime
CS Department of Experimental Radiation Oncology, University of Texas M.D. Anderson Cancer Center, Houston, Texas, USA.. lmilas@mdanderson.org
NC CA-06294 (NCI)
CA-16672 (NCI)
SO ONCOLOGY, (2003 May) 17 (5 Suppl 5) 15-24. Ref: 77
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030613
Last Updated on STN: 20031003
Entered Medline: 20031002

AB Radiation therapy has traditionally been the treatment of choice for locally or regionally advanced cancer, but its therapeutic efficacy is often hindered by limited tolerance of normal tissues and by tumor radioresistance. To improve therapeutic outcome, radiotherapy is frequently combined with chemotherapeutic drugs that are themselves cytotoxic and may sensitize cells to radiation. Solid evidence exists that administering standard chemotherapeutic agents during the course of radiotherapy (concurrent chemoradiotherapy) increases both local tumor control and patient survival in a number of cancer sites. These therapeutic improvements, however, have been achieved at the expense of considerable normal tissue toxicity. To improve chemoradiotherapy further, there have been extensive explorations of the potential of newer chemotherapeutic agents, including irinotecan (CPT-11, Camptosar) and other topoisomerase inhibitors. Preclinical studies have shown that these agents are potent radiosensitizers, providing a strong biologic rationale

for using these drugs in combination with radiotherapy. These studies also generated information critical for designing effective treatment schedules in clinical settings. The therapeutic efficacy of topoisomerase inhibitor-radiation combinations is currently being tested clinically. Recent advances in molecular biology have discovered many cellular molecules, including the cyclooxygenase-2 (COX-2) enzyme, that promote tumor cell survival and are responsible for tumor resistance to cytotoxic agents, and hence may serve as potential targets for augmentation of radio (or chemo) response. COX-2 is often overexpressed in premalignant lesions and cancer, and is involved in carcinogenesis, tumor growth, and metastatic spread. Preclinical studies provided solid evidence that inhibition of this enzyme with selective COX-2 inhibitors prevents carcinogenesis, slows the growth of established tumors, and enhances tumor response to radiation without appreciably affecting normal tissue radioresponse. The mechanisms of enhancement of tumor radioresponse involve direct actions on tumor cells and indirect actions, primarily on tumor vasculature. COX-2 inhibitors also improve tumor response to chemotherapeutic agents, including irinotecan. Additional therapeutic benefit was observed for celecoxib (Celebrex), a selective COX-2 inhibitor, consisting of a strong reduction in irinotecan-induced diarrhea. Thus, selective targeting of COX-2 may potentially improve radiotherapy, chemotherapy, or chemoradiotherapy--a therapeutic strategy that is currently being tested in clinical trials.

L74 ANSWER 34 OF 135 MEDLINE on STN
AN 2003447820 MEDLINE
DN 22871714 PubMed ID: 14508721
TI COX-2 inhibitors in oncology.
AU Haller Daniel G
CS University of Pennsylvania Cancer Center, Philadelphia, PA 19104, USA.
SO SEMINARS IN ONCOLOGY, (2003 Aug) 30 (4 Suppl 12) 2-8. Ref: 36
Journal code: 0420432. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030926
Last Updated on STN: 20031022
Entered Medline: 20031021

L74 ANSWER 35 OF 135 MEDLINE on STN
AN 2002696787 MEDLINE
DN 22345647 PubMed ID: 12457435
TI Cyclooxygenase 2 selective inhibitors in cancer treatment and prevention.
AU Menter David G
CS Department of Clinical Cancer Prevention, The University of Texas M.D. Anderson Cancer Center, Box 236, 1515 Holcombe Boulevard, Houston, TX 77030, USA.. dmenter@mdanderson.org
SO EXPERT OPINION ON INVESTIGATIONAL DRUGS, (2002 Dec) 11 (12) 1749-64. Ref: 150
Journal code: 9434197. ISSN: 1354-3784.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20021217
Last Updated on STN: 20030514
Entered Medline: 20030513
AB Prostaglandin synthesis by a number of enzymes is important at all stages during the genesis of cancer. The availability of prostaglandin H(2) as a substrate for prostaglandin production is a critical control point in its synthesis. Cyclooxygenase (COX) occurs in two forms (COX-1 and -2) and acts as the rate-limiting enzyme that generates prostaglandin H(2). COX-1 is produced as a steady-state enzyme, while COX-2 is heavily involved in inflammation and tumorigenesis. Differences in the catalytic sites of these enzymes are utilised to generate COX-2 selective inhibitors. Certain chemical characteristics of non-steroidal anti-inflammatory drugs and COX-2 selective inhibitors make some of these inhibitors more effective against COX-2 than others. Epidemiological, animal and preclinical data demonstrate the promise of non-steroidal anti-inflammatory drugs and COX-2 selective inhibitors as anticancer agents. Ongoing clinical trials are designed to determine the efficacy of non-steroidal anti-inflammatory drugs and COX-2 selective inhibitors in the prevention and treatment of many types of cancer.

L74 ANSWER 36 OF 135 MEDLINE on STN
AN 2002416372 MEDLINE
DN 22162068 PubMed ID: 12171541
TI Chemotherapeutic potential of curcumin for colorectal cancer.
AU Chauhan D P
CS Division of Gastroenterology, Department of Medicine, The University of California, San Diego, CA 92093-0688, USA.. dchauhan@ucsd.edu
SO CURRENT PHARMACEUTICAL DESIGN, (2002) 8 (19) 1695-706. Ref: 151
Journal code: 9602487. ISSN: 1381-6128.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20020813
Last Updated on STN: 20030125
Entered Medline: 20030124
AB Colorectal cancer is one of the leading causes of cancer deaths in the Western world. More than 56,000 newly diagnosed colorectal cancer patients die each year in the United States. Available therapies are either not effective or have unwanted side effects. Epidemiological data suggest that dietary manipulations play an important role in the prevention of many human cancers. Curcumin the yellow pigment in turmeric has been widely used for centuries in the Asian countries without any toxic effects. Epidemiological data also suggest that curcumin may be responsible for the lower rate of colorectal cancer in these countries. Curcumin is a naturally occurring powerful anti-inflammatory medicine. The anticancer properties of curcumin have been shown in cultured cells and animal studies. Curcumin inhibits lipooxygenase activity and is a specific inhibitor of cyclooxygenase-2 expression. Curcumin inhibits the initiation of carcinogenesis by inhibiting the cytochrome P-450 enzyme

activity and increasing the levels of glutathione-S-transferase. Curcumin inhibits the promotion/progression stages of carcinogenesis. The anti-tumor effect of curcumin has been attributed in part to the arrest of cancer cells in S, G2/M cell cycle phase and induction of apoptosis. Curcumin inhibits the growth of DNA mismatch repair defective colon cancer cells. Therefore, curcumin may have value as a safe chemotherapeutic agent for the treatment of tumors exhibiting DNA mismatch repair deficient and microsatellite instable phenotype. Curcumin should be considered as a safe, non-toxic and easy to use chemotherapeutic agent for colorectal cancers arise in the setting of chromosomal instability as well as microsatellite instability.

L74 ANSWER 37 OF 135 MEDLINE on STN
AN 2002734037 MEDLINE
DN 22384539 PubMed ID: 12495545
TI Radioprotection: the non-steroidal anti-inflammatory drugs (NSAIDs) and prostaglandins.
AU Lee Tat Khuen; Stupans Ieva
CS Center for Pharmaceutical Research, School of Pharmaceutical Molecular and Biomedical Sciences, University of South Australia, SA, 5000, Australia.
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (2002 Nov) 54 (11) 1435-45. Ref: 117
Journal code: 0376363. ISSN: 0022-3573.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20021227
Last Updated on STN: 20030524
Entered Medline: 20030523
AB Clinical and experimental studies of the acute and late effects of radiation on cells have enhanced our knowledge of radiotherapy and have led to the optimisation of radiation treatment schedules and to more precise modes of radiation delivery. However, as both normal and cancerous tissues have similar response to radiation exposure, radiation-induced injury on normal tissues may present either during, or after the completion of, the radiotherapy treatment. Studies on both NSAIDs and prostaglandins have indeed shown some evidence of radioprotection. Both have the potential to increase the survival of cells but by entirely different mechanisms. Studies of cell kinetics reveal that cells in the mitotic (M) and late G2 phases of the cell cycle are generally most sensitive to radiation compared with cells in the early S and G1/G0 phases. Furthermore, radiation leads to a mitotic delay in the cell cycle. Thus, chemical agents that either limit the proportion of cells in the M and G2 phases of the cell cycle or enhance rapid cell growth could in principle be exploited for their potential use as radioprotectors to normal tissue during irradiation. NSAIDs have been shown to exert anti-cancer effects by causing cell-cycle arrest, shifting cells towards a quiescence state (G0/G1). The same mechanism of action was observed in radioprotection of normal tissues. An increase in arachidonic acid concentrations after exposure to NSAIDs also leads to the production of an apoptosis-inducer ceramide. NSAIDs also elevate the level of superoxide dismutase in cells. Activation of heat shock proteins by NSAIDs increases cell survival by alteration of cytokine expression. A

role for NSAIDs with respect to inhibition of cellular proliferation possibly by an anti-angiogenesis mechanism has also been suggested. Several in-vivo studies have provided evidence suggesting that NSAIDs may protect normal tissues from radiation injury. Prostaglandins do not regulate the cell cycle, but they do have a variety of effects on cell growth and differentiation. PGE(2) mediates angiogenesis, increasing the supply of oxygen and nutrients, essential for cellular survival and growth. Accordingly, PGE(2) at sufficiently high plasma concentrations enhances cellular survival by inhibiting pro-inflammatory cytokines such as TNF-alpha and IL-1beta. Thus, PGE(2) acts as a modulator, rather than a mediator, of inflammation. Prospective studies have suggested the potential use of misoprostol, a PGE(1) analogue, before irradiation, in prevention of radiation-induced side effects. The current understanding of the pharmacology of NSAIDs and prostaglandins shows great potential to minimise the adverse effects of radiotherapy on normal tissue.

L74 ANSWER 38 OF 135 MEDLINE on STN
AN 2003007320 MEDLINE
DN 22401111 PubMed ID: 12512387
TI Angiogenesis as a target for cancer therapy.
AU Kaban Kerim; Herbst Roy S
CS Department of Thoracic Head and Neck Medical Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.
SO HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA, (2002 Oct) 16 (5) 1125-71. Ref: 299
Journal code: 8709473. ISSN: 0889-8588.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20030107
Last Updated on STN: 20030725
Entered Medline: 20030724
AB Antiangiogenic drugs are unique for having highly specific targets while carrying the potential to be effective against a wide variety of tumors. Moreover, some of the major limitations of cytotoxic therapies likely will be avoided by this entirely new class of anticancer weapons. After the realization of the potential advantages of antiangiogenic therapy, the field of angiogenesis research is growing exponentially. Still, there is much to learn about the machinery that tumors use to recruit new blood vessels, and the results of the clinical trials will show the best way to apply that knowledge for cancer therapy.

L74 ANSWER 39 OF 135 MEDLINE on STN
AN 2002211808 MEDLINE
DN 21942477 PubMed ID: 11945150
TI The role of cyclooxygenase inhibitors in cancer prevention.
AU Anderson William F; Umar Asad; Viner Jaye L; Hawk Ernest T
CS Gastrointestinal & Other Cancers Research Group, National Cancer Institute, Division of Cancer Prevention, EPN, Room 2141, 6130 Executive Boulevard, Bethesda, MD 20892-7317, USA.
SO CURRENT PHARMACEUTICAL DESIGN, (2002) 8 (12) 1035-62. Ref: 344
Journal code: 9602487. ISSN: 1381-6128.
CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200208
ED Entered STN: 20020412
Last Updated on STN: 20020827
Entered Medline: 20020826
AB Carcinogenesis results from the long-term accumulation of genetic and epigenetic aberrations at the molecular level, which are under constant selection pressure for growth advantage. Recognizing that cancer is the result of this long-term, multi-step process provides opportunities for molecularly targeted cancer prevention. Ideally, chemopreventive agents should be low in toxicity, morbidity, and cost. Several individual agents and agent combinations are currently under evaluation in the U.S. National Cancer Institute s (NCI) chemoprevention agent development program. Nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase (COX) -1 and -2 are among the most promising classes of agents for targeted molecular prevention.

L74 ANSWER 40 OF 135 MEDLINE on STN
AN 2002340395 MEDLINE
DN 22061313 PubMed ID: 12066226
TI Synergistic interaction between highly specific cyclooxygenase-2 inhibitor, MF-tricyclic and lovastatin in murine colorectal cancer cell lines.
AU Feleszko Wojciech; Jalili Ahmad; Olszewska Dominika; Mlynarczuk Izabela; Grzela Tomasz; Giermasz Adam; Jakobisiak Marek
CS Department of Immunology, Centre of Biostructure Research, The Medical University of Warsaw, Poland.. wfeleszk@ib.amwaw.edu.pl
SO ONCOLOGY REPORTS, (2002 Jul-Aug) 9 (4) 879-85.
Journal code: 9422756. ISSN: 1021-335X.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20020627
Last Updated on STN: 20030109
Entered Medline: 20030108
AB Statins, anti-hypercholesterolemic agents, have previously been reported to induce apoptosis and exert antitumor activity when combined with other antitumor agents. The potential of lovastatin in combination with highly specific COX-2 inhibitor (MF-tricyclic) to induce anti-proliferative activity against tumour cells was evaluated using the combination index (CI) method. Murine colorectal cancer (colon-26, CMT-93), melanoma (B16F10) and human bladder carcinoma cells (T24) were tested. Exposure of colon-26 and CMT-93 cells resulted in synergistic interactions in both cell lines with CI<1 for 20-80% inhibition of cell growth in both cell lines. This synergy was not observed in the B16F10 melanoma and T24 bladder carcinoma cells. MF-tricyclic (40 microg/ml), augmented lovastatin-induced apoptosis up to 2.5-fold in colon-26 cancer cells. Combination of a specific COX-2 inhibitor, MF-tricyclic, may increase antiproliferative effects of lovastatin in colon cancer cells and this effect was due to an augmented apoptosis.

L74 ANSWER 41 OF 135 MEDLINE on STN
AN 2003184931 MEDLINE
DN 22589633 PubMed ID: 12703233
TI Novel therapies for the treatment of non-small cell lung cancer.
AU Johnson David H; Schiller Joan H
CS Division of Hematology and Oncology, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, 777 Preston Research Building, Nashville, TN 37232-6307, USA.. david.johnson@mcmail.vanderbilt.edu
SO CANCER CHEMOTHERAPY AND BIOLOGICAL RESPONSE MODIFIERS, (2002) 20 763-86. Ref: 187
Journal code: 8812385. ISSN: 0921-4410.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030422
Last Updated on STN: 20030528
Entered Medline: 20030527
AB The management of advanced NSCLC remains a daunting challenge. However, new tools are available for treating this malignancy and continued progress is likely. The future is bright with a myriad of opportunities to exploit our ever-expanding knowledge of tumor biology. What is perhaps most needed, however, is development of new methods to prevent children and young adults from ever taking up the use of tobacco. In addition, we need new techniques to assist those who are already addicted to escape from tobacco's death grip. Sadly, most users of tobacco still fail to recognize the dangers of their habit. This needs to change!

L74 ANSWER 42 OF 135 MEDLINE on STN
AN 2002671110 MEDLINE
DN 22318931 PubMed ID: 12431470
TI The role of cyclooxygenase-2 (COX-2) in breast cancer, and implications of COX-2 inhibition.
AU Singh-Ranger G; Mokbel K
CS Breast Cancer Unit, St. George's Hospital Medical School, London, SW17 0QT, UK.
SO EUROPEAN JOURNAL OF SURGICAL ONCOLOGY, (2002 Nov) 28 (7) 729-37. Ref: 86
Journal code: 8504356. ISSN: 0748-7983.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021115
Last Updated on STN: 20030115
Entered Medline: 20030114
AB The cyclooxygenase (COX) enzyme system is composed of two isoenzymes, COX-1 and COX-2. Recent sources of experimental and epidemiological evidence suggest a significant role for the COX enzymes, particularly COX-2, in the pathogenesis of breast cancer. This has important implications for treatment of the disease. This article reviews the evidence for a relationship between the COX enzyme system and mammary

carcinogenesis, and discusses the likely therapeutic roles and potential pitfalls of COX inhibition.

L74 ANSWER 43 OF 135 MEDLINE on STN
AN 2002732886 MEDLINE
DN 22383131 PubMed ID: 12494894
TI COX-2, NSAIDs and human neoplasia. Part I: Colorectal neoplasms.
AU Nasir A; Fernandez P M; Chughtai O R; Kaiser H E
CS International Society for the Study of Comparative Oncology Inc., Silver Spring, Maryland 20901, USA.
SO IN VIVO, (2002 Nov-Dec) 16 (6) 501-9. Ref: 72
Journal code: 8806809. ISSN: 0258-851X.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20021227
Last Updated on STN: 20030514
Entered Medline: 20030513
AB Cyclooxygenase-2 (COX-2), the inducible cyclooxygenase isozyme involved in the conversion of arachidonic acid (AA) to biologically active prostanoids, has become the subject of intense interest during the last few years. The recent surge of interest stems from seminal studies that correlated elevated expression of COX-2 with tumor induction and progression, and epidemiological studies that correlated reduced risk of developing certain types of cancers with chronic use of non-steroidal anti-inflammatory agents (NSAIDs). Although these observations were first reported with colorectal cancer (CRC), similar findings have subsequently been made with other types of cancers. A wide spectrum of studies continue to be undertaken in both laboratory and clinical settings to elucidate the mechanisms underlying these anti-tumor effects of COX-2 for potential translation into cancer chemoprevention and therapy. The aim of this article is to present a review of COX genes, the prostaglandin-cyclooxygenase relationship, the role of COX-2 in carcinogenesis and the rationale for targeting COX-2 with NSAIDs for cancer chemoprevention. Special emphasis is given to the role of COX-2 expression in the genesis and progression of colorectal neoplasia, and its correlation with other pathological characteristics of CRC. Preliminary observations on COX-2 expression in inflammatory bowel disease (IBD)-related colorectal neoplasia are also presented.

L74 ANSWER 44 OF 135 MEDLINE on STN
AN 2003133447 MEDLINE
DN 22534473 PubMed ID: 12647986
TI Systemic therapy for advanced pancreatic cancer.
AU El-Rayes Basil F; Philip Philip A
CS Division of Haematology and Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, MI 48201, USA.
SO Expert Rev Anticancer Ther, (2002 Aug) 2 (4) 426-36. Ref: 78
Journal code: 101123358. ISSN: 1473-7140.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030322
Last Updated on STN: 20030430
Entered Medline: 20030429
AB Death from pancreatic cancer remains high with few long-term survivors. Systemic chemotherapy with 5-fluorouracil-based combinations had minimal impact on natural history of this disease. Several new agents with activity against pancreatic cancer have been identified over the past decade. Gemcitabine has modest activity in this disease. Combination chemotherapy trials incorporating gemcitabine, cisplatin, 5-fluorouracil, oxaliplatin, docetaxel or irinotecan show improved outcomes in objective response rates and survival that need to be confirmed in prospectively randomized studies. Advancement in the understanding of the biology of pancreatic cancer has helped identify several molecular targets for the development of novel therapies. Ongoing and future treatment regimens for pancreatic cancer will incorporate traditional cytotoxic drugs and novel targeted therapies.

L74 ANSWER 45 OF 135 MEDLINE on STN
AN 2003133443 MEDLINE
DN 22534469 PubMed ID: 12647982
TI Advanced NSCLC: from cytotoxic systemic chemotherapy to molecularly targeted therapy.
AU Hoang Tien; Schiller Joan H
CS Department of Medicine, University of Wisconsin Medical School, Madison 53792, USA.. txh@medicine.wisc.edu
SO Expert Rev Anticancer Ther, (2002 Aug) 2 (4) 393-401. Ref: 85
Journal code: 101123358. ISSN: 1473-7140.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030322
Last Updated on STN: 20030430
Entered Medline: 20030429
AB Approximately a third of non-small cell lung cancer patients present with disseminated disease at the time of diagnosis. For these patients, as well as those with recurrent disease, chemotherapy remains the mainstay of treatment. For several decades, researchers have attempted different combinations of drugs in search for the 'best' chemotherapy regimen. Despite the emergence of newer, 'third-generation' cytotoxic agents, success is still modest at best. Fortunately, new insights in tumor biology, leading to the design of molecularly targeted drugs, are opening a new era in cancer treatment. These novel agents target molecular pathways specifically found in cancer cells, thus maximizing the antitumor effect while minimizing toxicities on normal cells.

L74 ANSWER 46 OF 135 MEDLINE on STN
AN 2002220389 MEDLINE
DN 21842817 PubMed ID: 11853685
TI Is inhibition of cyclooxygenase required for the anti-tumorigenic effects of nonsteroidal, anti-inflammatory drugs (NSAIDs)? In vitro versus in vivo

results and the relevance for the prevention and treatment of cancer.
AU Raz Amiram
CS Department of Biochemistry, The George S. Wise Faculty of Life Sciences, Tel Aviv University, Israel.. amiraz@post.tau.ac.il
SO BIOCHEMICAL PHARMACOLOGY, (2002 Feb 1) 63 (3) 343-7. Ref: 35
Journal code: 0101032. ISSN: 0006-2952.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020418
Last Updated on STN: 20020426
Entered Medline: 20020425
AB Active research is being conducted to unravel the cellular mechanisms mediating the anti-tumorigenic effects of nonsteroidal anti-inflammatory drugs (NSAIDs) and their association with cyclooxygenase (COX) inhibition. The majority of NSAIDs inhibit either COX-1, COX-2, or both and exert their anti-COX, anti-inflammatory, and anti-tumorigenic effects in vivo in a parallel dose-dependent manner. The effects are seen at NSAID blood plasma concentrations of 0.1-5 microM. Significantly, the same compounds tested at the same concentrations in incubations with cultured tumor cells in vitro similarly inhibit COX activities but are devoid of anti-proliferative activity. Yet, at much higher concentrations (100-20,000 microM), these same NSAIDs do exert anti-proliferative effects in vitro due to apparent non-specific toxic effects, as evidenced by disruption of ion transport and mitochondrial oxidation in some cells. A small group of NSAIDs (e.g. sulindac) do not inhibit COX enzymes significantly but can reduce the synthesis of prostanoids by alternate mechanisms. One such mechanism is inhibition of agonist-stimulated phospholipase-mediated release of arachidonic acid from phospholipids leading to depressed synthesis of prostanoids, especially prostaglandin E(2) (PGE(2)). Another group of non-COX inhibitors are the R-isomers of NSAIDs, based on the structure of 2-arylpropionic acid. These compounds exert anti-proliferative effects in vivo, acting by an as yet undetermined mechanism. A possible caveat in these data is an R to S chiral transformation in vivo that would render the R-isomer effect as being due to the S-isomer generated in vivo from it. Demonstration of minimal or no R to S inversion under the experimental in vivo conditions employed is, therefore, a necessary control in these studies. The overall body of data supports the conclusion that, for COX-inhibiting NSAIDs, their anti-tumorigenic effect in vivo is due to, and depends upon, inhibition of tumor COX enzymes, primarily COX-2. The cellular effects seen when adding high concentrations of NSAIDs to tumor cells cultured in vitro and the mechanisms proposed to mediate these effects may not have substantial relevance to the mechanisms that mediate the effects of NSAIDs in vivo.

L74 ANSWER 47 OF 135 MEDLINE on STN
AN 2002125239 MEDLINE
DN 21849256 PubMed ID: 11859737
TI [Chemoprevention of colorectal cancer].
La chimioprevention du cancer colorectal.
AU Benamouzig R; Chaussade S
CS Service d'Hepato-gastroenterologie, Hopital Avicenne, 125, rue de Stalingrad, F93000 Bobigny.

SO PRESSE MEDICALE, (2002 Jan 26) 31 (3) 124-7. Ref: 30
Journal code: 8302490. ISSN: 0755-4982.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200203
ED Entered STN: 20020226
Last Updated on STN: 20020311
Entered Medline: 20020308
AB A NEW CONCEPT: Chemoprevention of cancer consists in the administration of chemical agents to prevent or inhibit carcinogenesis. This strategy can be applied at any stage of carcinogenesis. ASSESSMENT: The development of such agents relies on classical bases: phases I, II and III. The approach consists in assessing the effect of the substance tested in patients with history of resected adenomas of the colon and at high risk of relapse and/or family risk of colon cancer. THE PRINCIPLE AGENTS UNDER ASSESSMENT: Are aspirin, type 2 cyclo-oxygenase inhibitors, calcium, folic acid, certain vitamins, hormone replacement therapy for menopausal women and difluoromethylornithine (DFMO).

L74 ANSWER 48 OF 135 MEDLINE on STN
AN 2002389797 MEDLINE
DN 22133889 PubMed ID: 12138405
TI A role for cyclooxygenase-2 inhibitors in the prevention and treatment of cancer.
AU Howe Louise R; Dannenberg Andrew J
CS Departments of Cell & Developmental Biology and Medicine, Weill Medical College of Cornell University, New York, NY 10021, USA.
NC CA-89578-01 (NCI)
SO SEMINARS IN ONCOLOGY, (2002 Jun) 29 (3 Suppl 11) 111-9. Ref: 92
Journal code: 0420432. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200208
ED Entered STN: 20020725
Last Updated on STN: 20020815
Entered Medline: 20020814
AB Cyclooxygenase-2 (COX-2) is being intensively evaluated as a pharmacologic target for both the prevention and treatment of cancer. Aberrant COX-2 expression was initially described in colorectal cancers and has now been detected in many human tumors, including breast cancers. Strikingly, forced expression of COX-2 in murine mammary gland drives tumor formation. Moreover, knocking out COX-2 protects against the formation of intestinal and skin tumors in animal cancer models. Consistent with these findings, selective COX-2 inhibitors possess anticancer properties. For example, selective COX-2 inhibitors reduce the formation and growth of experimental breast and colon cancers. Importantly, selective COX-2 inhibitors do not inhibit platelet function and cause fewer gastrointestinal side effects (peptic ulcer disease) than traditional nonsteroidal anti-inflammatory drugs. Clinical trials are warranted to define the role of selective

COX-2 inhibitors in the prevention and treatment of cancer.

L74 ANSWER 49 OF 135 MEDLINE on STN
AN 2002080476 MEDLINE
DN 21665656 PubMed ID: 11807164
TI COX-2: a target for colon cancer prevention.
AU Marnett Lawrence J; DuBois Raymond N
CS A.B. Hancock Jr. Memorial Laboratory for Cancer Research, Center in Molecular Toxicology, Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.. marnett@toxicology.mc.vanderbilt.edu
NC CA 68485 (NCI)
ES 00267 (NIEHS)
P01 CA-77839 (NCI)
R01 CA-89450 (NCI)
R01 DK-47297 (NIDDK)
SO ANNUAL REVIEW OF PHARMACOLOGY AND TOXICOLOGY, (2002) 42 55-80. Ref: 140
Journal code: 7607088. ISSN: 0362-1642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020128
Last Updated on STN: 20020404
Entered Medline: 20020402
AB Disease prevention is one area that both public and governmental agencies strongly support owing to its potential for an improved lifestyle and a reduction in health care costs. In this review, we focus on the clinical development of one target for cancer prevention, the COX-2 enzyme. This provides an excellent example of how basic research in biochemistry and pharmacology can lead to translational studies and eventually to approval of a drug by the FDA for use as a chemopreventive agent in humans. It is hoped that, as the genome sequence is understood more clearly, other targets will emerge that will provide even more effective drugs for future cancer prevention.

L74 ANSWER 50 OF 135 MEDLINE on STN
AN 2002363165 MEDLINE
DN 22104216 PubMed ID: 12109806
TI Preoperative chemoradiation for locally advanced rectal cancer: emerging treatment strategies.
AU Crane Christopher H; Janjan Nora A; Mason Kathy; Milas Luka
CS Department of Radiation Oncology, The University of Texas, M.D. Anderson Cancer Center, Houston 77030, USA.. ccrane@mdanderson.org
NC CA06294 (NCI)
CA16672 (NCI)
SO ONCOLOGY, (2002 May) 16 (5 Suppl 5) 39-44. Ref: 38
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 200212
ED Entered STN: 20020712
Last Updated on STN: 20021221
Entered Medline: 20021220
AB Over the past decade, patients with locally advanced rectal cancer at The University of Texas M. D. Anderson Cancer Center have been managed with preoperative chemoradiation. Patients achieving a complete clinical response to preoperative chemoradiation have had better pelvic tumor control, sphincterpreservation, and overall survival than those with gross residual disease. Some patients achieving a complete clinical response have even had rectal-preserving surgery (full-thickness local excision). These results emphasize the importance of maximizing tumor response. Further improvement in response and survival could be achieved by using novel chemotherapeutic agents or through tumor-selective molecular targeting strategies that enhance the effects of chemotherapy, radiotherapy, or both. Irinotecan (CPT-11, Camptosar) is a novel chemotherapy agent being evaluated clinically as a radiosensitizing agent in rectal cancer. Inhibition of several molecular targets-such as epidermal growth factor receptor, ras oncogene activation, the cyclooxygenase-2 (COX-2) enzyme, and neoangiogenesis-appears to be tumor-selective in preclinical models. COX-2 expression has been shown to enhance cytotoxic therapy in preclinical models. In vitro and in vivo studies show that selective COX-2 inhibition enhances the effects of radiotherapy as well as chemotherapy. COX-2 is also markedly upregulated in human colorectal cancer and appears to be associated with adverse patient prognosis. Thus, integration of molecular targeting, such as COX-2 selective inhibition with existing chemoradiation approaches, may provide selective tumor radiosensitization and chemosensitization, resulting in improved pelvic control, sphincter preservation, and overall survival.

L74 ANSWER 51 OF 135 MEDLINE on STN
AN 2002359111 MEDLINE
DN 22096893 PubMed ID: 12102578
TI Potential role of selective COX-2 inhibitors in cancer management.
AU Dang Chau T; Shapiro Charles L; Hudis Clifford A
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.. dangc@mskcc.org
SO ONCOLOGY, (2002 May) 16 (5 Suppl 4) 30-6. Ref: 83
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 20020710
Last Updated on STN: 20021220
Entered Medline: 20021219
AB Tumorigenesis is a complex process, and understanding the mechanisms behind tumorigenesis is key to identifying effective targeted therapies. Prostaglandins are signaling lipophilic molecules derived from phospholipids that are involved in normal physiologic functions. However, overexpression of prostaglandins has been associated with tumorigenesis. Several epidemiologic studies have shown an inverse correlation between

the incidence of colon cancer and the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis. The NSAIDs target cyclooxygenases (COX), essential enzymes inprostaglandin production. Cyclooxygenase-2 (COX-2) is an inducible form of the enzyme that is usually not expressed in normal tissue. Because COX-2 is frequently overexpressed in premalignant lesions and neoplasms, specific COX-2 inhibitors have been investigatedas chemoprevention andpotential chemotherapeutic agents. There is now preclinical and early clinical data that suggest inhibitors of COX-2 may protect against colon, breast, lung, esophageal, and oral tumors. This paper will discuss evidence addressing the possible mechanistic contribution of COX-2 in tumorigenesis and will explore the link between COX-2 activity and carcinogenesis. The potential role of COX-2 inhibitors in the chemoprevention and treatment of various tumors will also be discussed. Clinical trials using targeted inhibitors of COX-2 will be critical in determining if COX-2 is a viable molecular target in cancer management.

L74 ANSWER 52 OF 135 MEDLINE on STN
AN 2002705392 MEDLINE
DN 22354752 PubMed ID: 12466642
TI New chemotherapeutic agents: update of major chemoradiation trials in solid tumors.
AU Curran Walter J
CS Department of Radiation Oncology, Jefferson Medical College, Philadelphia, Pa. 19107-5097, USA.. walter.curran@mail.tju.edu
SO ONCOLOGY, (2002) 63 Suppl 2 29-38. Ref: 32
Journal code: 0135054. ISSN: 0030-2414.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20021217
Last Updated on STN: 20030205
Entered Medline: 20030204
AB The institution of combined modality therapy for unresected solid tumors has resulted in significant improvements in tumor control and survival benefit compared with radiotherapy (RT) alone. A number of chemotherapy agents that can enhance the effectiveness of RT, such as cisplatin and 5-fluorouracil, are now considered standard treatment for patients with a number of cancer types. There is growing interest in a number of additional agents that have also been found to have radiosensitizing ability. These include paclitaxel, docetaxel, irinotecan, gemcitabine, and vinorelbine, as well as biologic agents. Other agents may be of value because they act to counter dose-limiting toxicities associated with RT. This article provides an update of some important, recently completed and ongoing clinical trials evaluating novel chemoradiation protocols, with examples taken primarily from studies conducted by the Radiation Therapy Oncology Group (RTOG). Theoretical approaches to the development of new agents and combined modality regimens are also discussed.

L74 ANSWER 53 OF 135 MEDLINE on STN
AN 2002227712 MEDLINE
DN 21961581 PubMed ID: 11965228

TI Celecoxib: a specific COX-2 inhibitor with anticancer properties.
AU Koki Alane T; Masferrer Jaime L
CS Pharmacia Corporation, Chesterfield, MO 63017, USA..
alane.t.koki@pharmacia.com
SO CANCER CONTROL, (2002 Mar-Apr) 9 (2 Suppl) 28-35. Ref: 106
Journal code: 9438457. ISSN: 1073-2748.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020420
Last Updated on STN: 20020614
Entered Medline: 20020613
AB In addition to the well-established pathophysiological role that COX-2 plays in inflammation, recent evidence implies that this isoform may also be involved in multiple biologic events throughout the tumorigenic process. Many epidemiological studies demonstrate that nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk of a wide range of tumors. Further, COX-2 is chronically overexpressed in many premalignant, malignant, and metastatic human cancers, and levels of overexpression have been shown to significantly correlate to invasiveness, prognosis, and survival in some cancers. Pharmacological studies consistently demonstrate that COX-2 inhibitors dose-dependently inhibit tumor growth and metastasis in various relevant animal models of cancer. Importantly, several investigators have also shown COX-2 inhibitors may act additively or synergistically with currently used cytotoxics and molecularly targeted agents. Here we present a broad overview of the growing evidence that COX-2 plays a pivotal role throughout oncogenesis and summarize the rationale to explore the use of COX-2 inhibitors for the prevention and/or treatment of cancer as a single agent or in combination with current anticancer modalities.

L74 ANSWER 54 OF 135 MEDLINE on STN
AN 2002274257 MEDLINE
DN 22009022 PubMed ID: 12014863
TI Celecoxib with chemotherapy in colorectal cancer.
AU Blanke Charles D
CS Oregon Health Sciences University, Portland 97201, USA.
SO ONCOLOGY, (2002 Apr) 16 (4 Suppl 3) 17-21. Ref: 32
Journal code: 8712059. ISSN: 0890-9091.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20020517
Last Updated on STN: 20021211
Entered Medline: 20021107
AB Cyclooxygenase-2 (COX-2) is the enzyme that normally synthesizes prostaglandins during an inflammatory response. Many primary and metastatic cancers express COX-2, and its presence is correlated with tumor angiogenesis, more invasive tumor phenotype, resistance to

apoptosis, and systemic immunosuppression. The expression of COX-2 is associated with a worse prognosis. Inhibition of prostaglandin synthesis may be beneficial in human malignancy. Regular consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) decreases the incidence of, and mortality rate resulting from, a number of types of gastrointestinal cancers. Premalignant colonic lesions regress following the administration of nonspecific COX inhibitors, such as sulindac (Clinoril). Advanced solid tumor patients treated with indomethacin (Indocin) survive twice as long as do such patients who receive supportive care alone. The U.S. Food and Drug Administration has approved specific COX-2 inhibitors for the treatment of arthritis, pain, and familial adenomatous polyposis. Preclinical studies show that these drugs block angiogenesis, suppress solid tumor metastases, and slow the growth of implanted gastrointestinal cancer cell lines. The COX-2 inhibitors have safely and effectively been combined with chemotherapeutic agents in experimental studies. Ongoing clinical trials are currently assessing the potential therapeutic role of COX-2 inhibitors in both prevention and treatment of a diverse range of human cancers.

L74 ANSWER 55 OF 135 MEDLINE on STN
AN 2002351066 MEDLINE
DN 22089123 PubMed ID: 12094332
TI Expression of target molecules in lung cancer: challenge for a new treatment paradigm.
AU Hirsch Fred R; Franklin Wilbur A; Bunn Paul A Jr
CS University of Colorado Cancer Center and Department of Medicine, University of Colorado Health Sciences Center, Denver, CO 80262, USA.
NC CA 46934-09 (NCI)
CA 58187-04 (NCI)
CA 85070 (NCI)
SO SEMINARS IN ONCOLOGY, (2002 Jun) 29 (3 Suppl 9) 2-8. Ref: 46
Journal code: 0420432. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020703
Last Updated on STN: 20020731
Entered Medline: 20020730
AB Lung cancer is the leading cause of cancer death in men and women in the United States, accounting for 28% of all cancer fatalities. More than two thirds of patients present with metastatic disease at the time of presentation. Despite improvements in chemotherapy and combined treatment modalities, the survival rate remains below 15%. However, recent advances in our understanding of the biology of lung cancer and carcinogenesis have led to the development of novel therapies directed at tumor-specific targets. These targets are crucial components in important pathways for cell growth, proliferation, and apoptosis. Strategies that interfere with these pathways include monoclonal antibodies directed at growth factors or their receptors, immunotoxins, ligand toxins, antisense molecules, ribozymes, and small-molecule inhibitors. Novel cell surface antigens are being used in vaccines developed to stimulate T-cell-specific immunity. The tumor cells also have specific survival requirements in their local environment that are necessary for invasion, angiogenesis, and metastases.

Many new therapeutic strategies are designed to interfere with these requirements. This article reviews many of these recent developments and new therapeutic possibilities; ideally, in the near future, these developments will be implemented in the treatment of lung cancer patients and in early detection and chemoprevention strategies.

L74 ANSWER 56 OF 135 MEDLINE on STN
AN 2001696158 MEDLINE
DN 21610847 PubMed ID: 11745453
TI Is COX-2 inhibition a panacea for cancer prevention?.
AU Vainio H
CS Unit of Chemoprevention, International Agency for Research on Cancer, Lyon, France.. vainio@iarc.fr
SO INTERNATIONAL JOURNAL OF CANCER, (2001 Dec 1) 94 (5) 613-4. Ref: 20
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 20011218
Last Updated on STN: 20020125
Entered Medline: 20020103
AB The epidemiologic evidence and rodent studies suggest strongly that nonselective inhibitors of cyclooxygenase (COX) enzymes such as aspirin, inhibiting both COX-1 and COX-2 isoforms, reduce the incidence of and mortality from intestinal tumors. Genetically manipulated animals show that both Cox-1 and Cox-2 disruptions decrease the tumor yield, both in genetically predisposed and in carcinogen-treated mice. The mechanisms by which COX-1 and COX-2 deficiency decrease tumorigenesis are still unknown. Cox-2 overexpression increased the tumor yield in mammary glands of the multiparous, but not virginal female transgenic mice using the murine mammary tumor virus promoter. The Cox-2 protein was strongly induced during pregnancy and lactation. These data suggest that Cox-2 overexpression may be an important target for cancer chemoprevention. This finding was supported by the observed cancer-preventive effects of the COX-2-specific inhibitors in humans and in rodents. However, based on the available data, we cannot totally attribute the cancer preventive effects of nonsteroidal antiinflammatory drugs (NSAIDs) to COX-2 alone-even COX-1 may have an important role in cancer prevention as suggested by the Cox-1-deficient Min mice. It is likely that COX-1 plays a more important role in NSAID-induced toxicity in humans, such as in gastric ulcer formation-but inhibition of COX-2 may not be without toxic manifestations either, as suggested by the poor survival of the Cox-2-nulled mice. Combinations of COX-2 inhibitors with other agents that target other pathways in carcinogenesis may be a more efficacious and a less toxic strategy in cancer chemoprevention.

L74 ANSWER 57 OF 135 MEDLINE on STN
AN 2001421560 MEDLINE
DN 21364013 PubMed ID: 11470927
TI Familiar drugs may prevent cancer.
AU Sharma R A; Gescher A J; O'Byrne K J; Steward W P

CS Oncology Department, University of Leicester, Leicester Royal Infirmary, Leicester LE1 5WW, UK.. ras20@le.ac.uk
SO POSTGRADUATE MEDICAL JOURNAL, (2001 Aug) 77 (910) 492-7. Ref: 60
Journal code: 0234135. ISSN: 0032-5473.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200109
ED Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913
AB Despite positive results in large scale chemoprevention trials, many physicians are unaware of the potential cancer preventive properties of drugs in common usage. The antioestrogen tamoxifen and the selective cyclo-oxygenase-2 inhibitor celecoxib have been licensed in the USA for the chemoprevention of breast and colorectal cancers respectively in selected high risk individuals. Similarly, folate and retinol have been shown to decrease the incidence of colorectal cancer and squamous cell carcinoma of the skin respectively in large scale intervention trials. Other retinoids have proved efficacious in the tertiary chemoprevention of cancers of the breast and head/neck. Epidemiological evidence also exists in favour of aspirin, non-steroidal anti-inflammatory drugs, and angiotensin converting enzyme inhibitors preventing certain cancers. Phytochemicals may represent less toxic alternatives to these agents. Although some of these drugs are available without prescription and most are not yet licensed for use in cancer chemoprevention, physicians and students of medicine should be aware of this accumulating evidence base. Practitioners should be amenable to patient referral to discuss complex issues such as risk estimation or potential benefit from intervention.

L74 ANSWER 58 OF 135 MEDLINE on STN
AN 2001571419 MEDLINE
DN 21535134 PubMed ID: 11677654
TI Cyclooxygenase-2 (COX-2) enzyme inhibitors as potential enhancers of tumor radioresponse.
AU Milas L
CS Department of Experimental Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030-4009, USA.
SO SEMINARS IN RADIATION ONCOLOGY, (2001 Oct) 11 (4) 290-9. Ref: 58
Journal code: 9202882. ISSN: 1053-4296.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011029
Last Updated on STN: 20020123
Entered Medline: 20011207
AB Cyclooxygenase-2 (COX-2) is an enzyme induced by a variety of factors including tumor promoters, cytokines, growth factors and hypoxia. It is involved in the metabolic conversion of arachidonic acid to prostanoids, primarily in inflammatory states and tumors. In normal tissues,

prostanoids are synthesized by COX-1, and they exert numerous homeostatic physiologic functions. COX-2 overexpression is linked to carcinogenesis, maintenance of progressive tumor growth and facilitation of metastatic spread. COX-2 and its products may act as protectors against cell damage by ionizing radiation. I describe findings showing that inhibition of COX-2 or prostanoids by selective COX-2 inhibitors or commonly used nonsteroidal antiinflammatory drugs (NSAIDs) has antitumor activity and may improve tumor response to radiation without significantly affecting normal tissue radioresponse. COX-2 inhibitors and radiation interact in multiple complex ways, with the enzyme inhibitor directly or indirectly augmenting tumor cell destruction by radiation. COX-2 represents a potential molecular target for improvement of cancer radiotherapy. Copyright 2001 by W.B. Saunders Company

L74 ANSWER 59 OF 135 MEDLINE on STN
AN 2001168252 MEDLINE
DN 21166787 PubMed ID: 11268709
TI The prevention of breast cancer: an overview.
AU Leris C; Mokbel K
CS South East Thames Training Programme, London, UK.
SO CURRENT MEDICAL RESEARCH AND OPINION, (2001) 16 (4) 252-7. Ref: 30
Journal code: 0351014. ISSN: 0300-7995.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712
AB The role of lifestyle modifications, antioestrogens, cyclo-oxygenase-2 inhibitors and prophylactic mastectomy in reducing breast cancer is reviewed. It is concluded that avoiding postmenopausal obesity and regular physical activity are simple measures that seem to reduce breast cancer risk. There is no conclusive evidence that dietary modification and vitamin supplementation significantly reduce the risk of breast cancer. The evidence suggests that tamoxifen significantly reduces the risk of breast cancer in women at increased risk, but whether it reduces breast cancer mortality remains unknown. Ongoing clinical trials may prove that raloxifene is superior to tamoxifen in breast cancer prevention due to its anti-oestrogenic effects on the endometrium. Bilateral prophylactic mastectomy reduces the risk of breast cancer by 90% in high risk women.

L74 ANSWER 60 OF 135 MEDLINE on STN
AN 2002053265 MEDLINE
DN 21637359 PubMed ID: 11779086
TI Approach to angiogenesis inhibition based on cyclooxygenase-2.
AU Masferrer J
CS Pharmacia Corporation, St. Louis, Missouri 63167, USA.
SO CANCER JOURNAL, (2001 Nov-Dec) 7 Suppl 3 S144-50. Ref: 38
Journal code: 100931981. ISSN: 1528-9117.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020125
Last Updated on STN: 20020321
Entered Medline: 20020320
AB Two cyclooxygenase (COX) isoforms have been identified: COX-1 and COX-2. COX-1 is the constitutively expressed form of the enzyme and is ubiquitous in its distribution. COX-2 is inducible and is present in inflammatory foci, tumors, and neovasculature. Expression of COX-2 appears to be important in tumor promotion, growth, and metastasis. It is up-regulated in a variety of premalignant disorders and malignancies. COX inhibitors have a major role in the treatment of inflammation and pain. Epidemiologic evidence in patients who take nonsteroidal anti-inflammatory drugs links COX inhibition with decreases in malignant esophageal, stomach, colon, lung, and breast tumors. Nonselective COX inhibitors have demonstrated efficacy in control of familial adenomatous polyposis, a disorder associated with the development of thousands of benign intestinal polyps. The selective COX-2 inhibitor celecoxib (Celebrex, Pharmacia) has been shown to reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis as an adjunct to usual care. Celecoxib has recently been approved for this indication and offers the potential for equivalent or greater efficacy than that seen with nonselective COX inhibitors but without the gastrointestinal mucosal toxicity and the inhibition of platelet function associated with those agents. Angiogenesis is a feature of both benign and malignant disease. Because COX-2 is up-regulated in the neovasculature of the rheumatoid pannus and in malignant tumors and their surrounding stroma, selective COX-2 inhibitors may be able to modify the progression of these disorders through the control of angiogenesis.

L74 ANSWER 61 OF 135 MEDLINE on STN
AN 2002069847 MEDLINE
DN 21653734 PubMed ID: 11795429
TI Inhibition of cyclooxygenase-2: an approach to preventing cancer of the upper aerodigestive tract.
AU Dannenberg A J; Altorki N K; Boyle J O; Lin D T; Subbaramaiah K
CS Department of Medicine, New York Presbyterian Hospital and Weill Medical College of Cornell University, New York 10021, USA..
ajdannen@med.cornell.edu
NC R01 CA82578 (NCI)
T32 CA09685 (NCI)
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2001 Dec) 952 109-15. Ref: 52
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020125
Last Updated on STN: 20020214
Entered Medline: 20020213
AB Multiple lines of evidence suggest that cyclooxygenase-2 (COX-2), an

inducible form of COX, represents a potential pharmacologic target to prevent cancer. Key data suggesting a causal relationship between increased COX-2 activity and carcinogenesis and possible mechanisms of action of COX-2 in this context will be discussed. The possibility that COX-2 represents a pharmacological target for preventing upper aerodigestive cancers (head and neck, lung) will be emphasized. Importantly, clinical trials have been initiated to assess the chemopreventive properties of selective COX-2 inhibitors.

L74 ANSWER 62 OF 135 MEDLINE on STN
AN 2002069864 MEDLINE
DN 21653733 PubMed ID: 11795446
TI The future of colon cancer prevention.
AU Umar A; Viner J L; Hawk E T
CS Gastrointestinal & Other Cancers Research Group, National Cancer Institute, Division of Cancer Prevention, EPN, Bethesda, Maryland 20892-7317, USA.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2001 Dec) 952 88-108. Ref: 138
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020125
Last Updated on STN: 20020214
Entered Medline: 20020213
AB Chemoprevention science is in flux owing to rapid advances in postgenomic technology. We have witnessed enormous advances in the areas of early detection and molecular profiling of colorectal carcinogenesis; however, unique interpretive and technologic challenges persist. Neoplastic hallmarks must be iteratively tested and validated as markers of risk, targets for intervention, and/or markers of response in order to expedite the development of preventive interventions. In this review, we highlight several of the technologies that are revolutionizing our understanding of carcinogenesis and our approach to colorectal cancer prevention.

L74 ANSWER 63 OF 135 MEDLINE on STN
AN 2001179575 MEDLINE
DN 21090585 PubMed ID: 11166005
TI Doubt and certainty about nonsteroidal anti-inflammatory drugs in the year 2000: a multidisciplinary expert statement.
AU Hawkey C J; Lanas A I
CS Division of Gastroenterology, University Hospital Nottingham, Queen's Medical Centre, Nottingham, United Kingdom. (Sardinia NSAID meeting).
SO AMERICAN JOURNAL OF MEDICINE, (2001 Jan 8) 110 (1A) 79S-100S. Ref: 241
Journal code: 0267200. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200103

ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L74 ANSWER 64 OF 135 MEDLINE on STN
AN 2001416460 MEDLINE
DN 21358066 PubMed ID: 11465540
TI Discovery and design of selective cyclooxygenase-2 inhibitors as non-ulcerogenic, anti-inflammatory drugs with potential utility as anti-cancer agents.
AU Kalgutkar A S; Zhao Z
CS Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
SO Curr Drug Targets, (2001 Mar) 2 (1) 79-106. Ref: 188
Journal code: 100960531. ISSN: 1389-4501.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010813
Last Updated on STN: 20030401
Entered Medline: 20010809
AB The recent marketing of two selective cyclooxygenase-2 (COX-2) inhibitors, celecoxib and rofecoxib is remarkable considering that COX-2 was only discovered eight years ago as a growth factor- and cytokine-inducible gene. Concomitant with these pharmaceutical successes is the advances in our understanding of the molecular and structural basis for selective COX-2 inhibition. This review provides a perspective on the ongoing structure-activity relationship (SAR) efforts in the search of COX-2-specific inhibitors with particular reference to their structural basis for isozyme-specific inhibition. In addition to the existing inhibitor classes, this review will also highlight many novel structural classes which have recently emerged due to a better understanding of the active site differences between the two isozymes with a special emphasis on the modification of the well-established non-steroidal anti-inflammatory drug (NSAID) scaffold. In addition to its role in inflammation, recent studies suggest that COX-2-derived prostaglandins may play a pivotal part in the maintenance of tumor viability, growth, and metastasis. In this review, we summarize the NSAID epidemiological evidence, studies demonstrating overexpression of COX-2 in multiple human tumors and pharmacological evidence in animal models, which indicate that COX-2 inhibitors could be used in the prevention or treatment of a broader range of disease.

L74 ANSWER 65 OF 135 MEDLINE on STN
AN 2001179572 MEDLINE
DN 21090582 PubMed ID: 11166002
TI Nonsteroidal anti-inflammatory drugs and the gastrointestinal tract. Extent, mode, and dose dependence of anticancer effects.
AU Sjodahl R
CS Department of Surgery, University Hospital, Linkoping, Sweden.
SO AMERICAN JOURNAL OF MEDICINE, (2001 Jan 8) 110 (1A) 66S-69S. Ref: 30
Journal code: 0267200. ISSN: 0002-9343.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329
AB Regular intake of aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a decreased incidence of colorectal, esophageal, gastric, and lung cancer. The relative risk of colorectal cancer is about 0.6 in large cohort studies--in other words, the risk is reduced by 40%. Also, in experimental models, the frequency of colonic cancer is reduced by NSAIDs. Both human and experimental tumors contain increased amounts of prostaglandin E(2), which may have a role in the accelerated proliferation taking place in tumor tissue. This may be the result of activation of cyclooxygenase-2 (COX-2) in response to mitogens and growth factors, for example, which will result in an increased production of prostaglandins. The current theory is that the mechanism for the suppressor effect of NSAIDs on carcinogenesis is COX-2 inhibition. However, reliable data on the dose of aspirin or other NSAIDs for optimal benefit for tumor suppression are lacking, and it is still premature to give general recommendations on using NSAIDs for chemoprevention of gastrointestinal cancer.

L74 ANSWER 66 OF 135 MEDLINE on STN
AN 2002069861 MEDLINE
DN 21653730 PubMed ID: 11795443
TI Beyond tamoxifen new endpoints for breast cancer chemoprevention, new drugs for breast cancer prevention.
AU Fabian C J; Kimler B F
CS University of Kansas Medical Center, Kansas City 66160-7320, USA.. cfabian@kumc.edu
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2001 Dec) 952 44-59. Ref: 113
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020125
Last Updated on STN: 20020214
Entered Medline: 20020213
AB Although tamoxifen appears to markedly reduce breast cancer risk in women with a prior diagnosis of atypical hyperplasia or in situ carcinoma, it is not clear what other groups of women receive substantial benefit. Major breast chemoprevention priorities are to (1) develop new agents that (a) have fewer side effects, (b) are effective in ER--as well as tamoxifen-resistant precancerous tissue, and (c) are compatible with hormone therapy; and (2) develop efficient clinical strategies including prognostic and predictive morphologic and molecular biomarkers. Breast tissue may be repeatedly sampled for evidence of intraepithelial neoplasia by fine needle aspiration, ductal lavage, or needle biopsy to select

candidates at highest short-term risk as well as to monitor response in small proof of principle studies prior to a large cancer incidence trial. Molecular marker expression may also be used to select a cohort most likely to respond to a particular agent. A large number of new agents are attractive as potential prevention agents and some are already in clinical prevention testing. Compounds which should be effective in ER + precancerous tissue but may have a better side-effect profile include new selective estrogen receptor modulators which lack uterine estrogen agonist activity, isoflavones, aromatase inactivators/inhibitors for postmenopausal women, and gonadotropin-releasing hormone regimens for premenopausal women. Retinoids, rexinoids, and deltanoids may be efficacious in ER+ tissue resistant to tamoxifen. Agents which should theoretically have activity in ER- or ER+ precancerous tissue include polyamine synthesis inhibitors, tyrosine kinase inhibitors, combined demethylating agents and histone deacetylase inhibitors, as well as metalloprotease and angiogenesis inhibitors. Sample Phase I and Phase II clinical trial designs are reviewed using modulation of molecular markers and breast intraepithelial neoplasia as the major endpoints.

L74 ANSWER 67 OF 135 MEDLINE on STN
AN 2001379145 MEDLINE
DN 21329125 PubMed ID: 11435450
TI Cyclooxygenase-selective inhibition of prostanoid formation: transducing biochemical selectivity into clinical read-outs.
AU Patrono C; Patrignani P; Garcia Rodriguez L A
CS Department of Medicine and Aging, University of Chieti G. D'Annunzio School of Medicine, Chieti, Italy.. cpatrono@unich.it
SO JOURNAL OF CLINICAL INVESTIGATION, (2001 Jul) 108 (1) 7-13. Ref: 31
Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200108
ED Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

L74 ANSWER 68 OF 135 MEDLINE on STN
AN 2001088511 MEDLINE
DN 20516109 PubMed ID: 11060781
TI Squalene: potential chemopreventive agent.
AU Smith T J
CS University of South Carolina, College of Pharmacy, Coker Life Sciences, 700 Sumter Street, Columbia, SC 29208, USA.. smithtj@pharm.sc.edu
SO EXPERT OPINION ON INVESTIGATIONAL DRUGS, (2000 Aug) 9 (8) 1841-8. Ref: 57
Journal code: 9434197. ISSN: 1354-3784.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medline: 20010118

AB Squalene is a triterpene that is an intermediate of the cholesterol biosynthesis pathway and it can be obtained from the diet. Olive oil contains 0.2-0.7% squalene. The average intake of squalene is 30 mg/day in the United States, however, when consumption of olive oil is high, the intake of squalene can reach 200-400 mg/day as observed in Mediterranean countries. The decreased risk for various cancers associated with high olive oil consumption may be due to the presence of squalene. Experimental studies have shown that squalene can effectively inhibit chemically-induced colon, lung and skin tumourigenesis in rodents. The protective effect is observed when squalene is given before and/or during carcinogen treatment. The mechanisms involved for the chemopreventive activity of squalene may include inhibition of Ras farnesylation, modulation of carcinogen activation and anti-oxidative activities. However, several factors must be taken into consideration when the evidence for the inhibition of carcinogenesis by squalene is examined, these include the effective dose used and the time of exposure. The information obtained is from animal bioassays and the long-term effects from consuming increased levels of squalene are not known. Although animal studies have enhanced our understanding of the possible action of squalene in decreasing carcinogenesis, one must apply caution in extrapolating the information obtained in animal studies to humans, because of possible species differences. In order to evaluate the overall implications of squalene to human cancer prevention, further studies are needed to fully identify its protective effects, as well as possible detrimental effects.

L74 ANSWER 69 OF 135 MEDLINE on STN
AN 2001015756 MEDLINE
DN 20401244 PubMed ID: 10944947
TI Recent studies on anti-angiogenesis in cancer therapy.
AU Kishi K; Milas L; Hunter N; Sato M
CS Department of Radiology, Wakayama Medical College.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2000 Aug) 58 (8) 1747-62. Ref: 98
Journal code: 0420546. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
FS Priority Journals
EM 200010
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001031

AB Angiogenesis is known to be a critical process for the tumor growth and metastasis. There are many indigenous role-players in tumor angiogenesis and anti-angiogenesis, where tumor-host interaction may work. A lot of agents with anti-angiogenic activity have been developed for anti-cancer treatment. Several agents including Marimastat, Primostat, Neovastat, Bay-12-9566m, Interferon-alpha, SU101, retinoids, and IM862, are/were under phase-three study. There are still many future-promising results of basic or clinical studies on inhibitors of MMPs, and inhibitors of VEGF/R, Endostatin, somatostatin analogues, COX-2 inhibitors, and others. Most of the combination treatments of antiangiogenetic agent and conventional

anticancer agents therapy, or radiation therapy as we reported, showed relatively small or minute increase in toxicity of these cytotoxic treatments.

L74 ANSWER 70 OF 135 MEDLINE on STN
AN 2000452214 MEDLINE
DN 20462136 PubMed ID: 11006874
TI [Primary prevention of sporadic colorectal carcinoma by diet modification and drugs?].
Primarpravention des sporadischen kolorektalen Karzinoms durch Ernahrungsmodifikation und Medikamente?.
AU Scheppach W; Melcher R; Luhrs H; Menzel T
CS Medizinische Universitatsklinik Wurzburg.. w.scheppach@medizin.uni-wuerzburg.de
SO INTERNIST, (2000 Sep) 41 (9) 868-75. Ref: 58
Journal code: 0264620. ISSN: 0020-9554.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 200010
ED Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001019

L74 ANSWER 71 OF 135 MEDLINE on STN
AN 2000156143 MEDLINE
DN 20156143 PubMed ID: 10688873
TI Chemoprevention of cancer.
AU Sporn M B; Suh N
CS Department of Pharmacology, Dartmouth Medical School, Hanover, NH 03755, USA.. michael.b.sporn@dartmouth.edu
SO CARCINOGENESIS, (2000 Mar) 21 (3) 525-30. Ref: 47
Journal code: 8008055. ISSN: 0143-3334.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000411
AB In this short article, we review the conceptual basis for chemoprevention of cancer, the proven clinical efficacy of this concept, and current trends to develop new chemopreventive agents based on understanding of their mechanisms of action. Four classes of new agents, namely selective inhibitors of cyclooxygenase-2, selective estrogen receptor modulators, rexinoids (retinoids that bind selectively to the receptors known as RXRs) and ligands for the peroxisome proliferator-activated receptor-gamma are discussed in detail. The importance of developing totally new classes of chemopreventive agents is stressed, with particular emphasis on the potential usefulness of new synthetic triterpenoids derived from naturally occurring molecules.

L74 ANSWER 72 OF 135 MEDLINE on STN
AN 2000511059 MEDLINE
DN 20518292 PubMed ID: 11064689
TI Cancer chemoprevention: a clinical reality.
AU Sharma R A
CS MRC Toxicology Unit, University of Leicester, UK.. ras20@le.ac.uk
SO JOURNAL OF THE ROYAL SOCIETY OF MEDICINE, (2000 Oct) 93 (10) 518-20. Ref: 33
Journal code: 7802879. ISSN: 0141-0768.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001109

L74 ANSWER 73 OF 135 MEDLINE on STN
AN 2001139844 MEDLINE
DN 21041910 PubMed ID: 11201293
TI The role of cyclooxygenase and lipoxygenase in cancer chemoprevention.
AU Cuendet M; Pezzuto J M
CS Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, and University of Illinois Cancer Center, University of Illinois at Chicago, 60612, USA.
NC P01 CA48112 (NCI)
SO DRUG METABOLISM AND DRUG INTERACTIONS, (2000) 17 (1-4) 109-57. Ref: 274
Journal code: 8904736. ISSN: 0792-5077.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010308
AB The involvement of prostaglandins (PGs) and other eicosanoids in the development of human cancer has been known for over two decades. Importantly, an increase in PG synthesis may influence tumor growth in human beings and experimental animals, and numerous studies have illustrated the effect of PG synthesis on carcinogen metabolism, tumor cell proliferation and metastatic potential. PGs produced by cyclooxygenases (COXs) are represented by a large series of compounds that mainly enhance cancer development and progression, acting as carcinogens or tumor promoters, with profound effects on carcinogenesis. Further investigations suggest that arachidonic acid (AA) metabolites derived from lipoxygenase (LOX) pathways play an important role in growth-related signal transduction, implying that intervention through these pathways should be useful for arresting cancer progression. We discuss here the implications of COX and LOX in colon, pancreatic, breast, prostate, lung, skin, urinary bladder and liver cancers. Select inhibitors of COX and LOX

are described, including nonsteroidal antiinflammatory drugs (NSAIDs), selective COX-2 inhibitors, curcumin, tea, silymarin and resveratrol, as well as a method useful for evaluating inhibitors of COX. Although a substantial amount of additional work is required to yield a better understanding of the role of COX and LOX in cancer chemoprevention, it is clear that beneficial therapeutic effects can be realized through drug-mediated modulation of these metabolic pathways.

L74 ANSWER 74 OF 135 MEDLINE on STN
AN 2001153392 MEDLINE
DN 21029327 PubMed ID: 11191059
TI The contributions of cyclooxygenase-2 to tumor angiogenesis.
AU Gately S
CS Department of Medicine, Northwestern University Medical School, Chicago, IL, USA.. sg@northwestern.edu
SO CANCER AND METASTASIS REVIEWS, (2000) 19 (1-2) 19-27. Ref: 144
Journal code: 8605731. ISSN: 0891-9992.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010322
AB Cyclooxygenase-2 (COX-2) is an immediate early response gene that can be induced by a variety of tumor promoters, cytokines, growth factors and hypoxia. COX-2 overexpression is linked to all stages of carcinogenesis with the enzyme localized to the neoplastic cells, microvascular endothelial cells, and stromal fibroblasts. The contributions of COX-2 in tumor angiogenesis include: (a) the increased expression of the proangiogenic growth factor VEGF; (b) the production of the eicosanoid products thromboxane A2, PGE2 and PGI2 that can directly stimulate endothelial cell migration and growth factor-induced angiogenesis; and potentially, (c) the inhibition of endothelial cell apoptosis by stimulation of Bcl-2 or Akt activation. Selective pharmacological inhibitors of COX-2 as angiosuppressive agents could have therapeutic benefit in the treatment of neoplastic disease from prevention through treatment of advanced metastatic disease. These agents are safe and well tolerated and can be added to chemotherapy and radiation therapy where angiogenesis inhibitors appear to provide at least additive therapeutic benefit.

L74 ANSWER 75 OF 135 MEDLINE on STN
AN 2000094339 MEDLINE
DN 20094339 PubMed ID: 10630643
TI The role of cyclooxygenases in inflammation, cancer, and development.
AU Williams C S; Mann M; DuBois R N
CS Department of Medicine, The Vanderbilt Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee 37232-2279, USA.
NC DK 47297 (NIDDK)
P030 ES-00267-29 (NIEHS)
PO1CA-77839 (NCI)
SO ONCOGENE, (1999 Dec 20) 18 (55) 7908-16. Ref: 80
Journal code: 8711562. ISSN: 0950-9232.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000120
AB The cyclooxygenase (COX) enzymes catalyze a key step in the conversion of arachidonate to PGH2, the immediate substrate for a series of cell specific prostaglandin and thromboxane synthases. Prostaglandins play critical roles in numerous biologic processes, including the regulation of immune function, kidney development, reproductive biology, and gastrointestinal integrity. There are two COX isoforms, which differ mainly in their pattern of expression. COX-1 is expressed in most tissues, whereas COX-2 usually is absent, but is induced by numerous physiologic stimuli. Surprisingly, disruption of Cox1 (Ptgs1) in the mouse did not result in gastrointestinal abnormalities. cox-2 (Ptgs2) null mice show reproductive anomalies and defects in kidney development. Epidemiologic, animal, and human data indicate that NSAIDs, inhibitors of cyclooxygenase, are chemopreventive for colon cancer. COX-2 is overexpressed in 50% of benign polyps and 80-85% of adenocarcinomas. Offspring from cox-2 null by Apcdelta716 matings exhibit an 86% reduction in polyp number when compared to offspring from control animals, thus providing genetic evidence that COX-2 contributes to tumor formation or growth. The in vivo mechanism by which COX-2 affects tumor growth has not been determined. It is possible that both tumor and stromally derived COX-2 could influence tumor angiogenesis and/ or immune function.

L74 ANSWER 76 OF 135 MEDLINE on STN
AN 2000003661 MEDLINE
DN 20003661 PubMed ID: 10533468
TI Non steroidal anti-inflammatory drugs and colorectal cancer: is there a way forward?.
AU Kubba A K
CS University Department of Surgery, University of Newcastle upon Tyne, U.K.
SO EUROPEAN JOURNAL OF CANCER, (1999 Jun) 35 (6) 892-901. Ref: 110
Journal code: 9005373. ISSN: 0959-8049.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991105
AB Non steroidal anti-inflammatory drugs (NSAIDs) have diverse clinical applications through modulation of oxidative processes and cell signalling. Observations that these agents may inhibit human colorectal carcinogenesis have produced great excitement. However, comparative data relating to their chemopreventative effectiveness or to relevant mechanisms of action remains unclear. This review considers the clinical and epidemiological evidence for colorectal tumour prevention by NSAIDs

against current concepts of drug mechanisms. We also propose areas of further research for potential therapeutic advancement.

L74 ANSWER 77 OF 135 MEDLINE on STN
AN 2000131762 MEDLINE
DN 20131762 PubMed ID: 10667110
TI [Selective cyclooxygenase-2 (COX-2) inhibitors: importance and limitations].
Inhibiteurs selectifs de la cyclooxygenase de type 2 (COX-2): interets et limites.
AU Pairet M; Netter P
CS Boehinger Ingelheim Pharma KG, Dept of Pulmonary Research, Ingelheim am Rhein, Germany.
SO THERAPIE, (1999 Jul Aug) 54 (4) 433-45. Ref: 140
Journal code: 0420544. ISSN: 0040-5957.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200003
ED Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000316
AB The discovery of an inducible form of cyclooxygenase (COX-2) requires a refinement of the theory that inhibition of cyclooxygenase activity explains both therapeutic effects and side-effects of non-steroidal anti-inflammatory drugs (NSAIDs). Selective COX-2 inhibitors have demonstrated in clinical trials a significantly better gastrointestinal tolerability than classical NSAIDs, for the same anti-inflammatory activity. Their tolerability in patients with active ulcer or with a recent history of ulcer as well as in patients suffering from cardiovascular or renal diseases has still to be investigated in detail. Their therapeutic potential in several new indications, including pre-term labour, colorectal cancer and Alzheimer's disease, is currently being investigated.

L74 ANSWER 78 OF 135 MEDLINE on STN
AN 2000024263 MEDLINE
DN 20024263 PubMed ID: 10560473
TI Preventing heart disease and cancer. What randomized, primary-prevention studies show.
AU Lush D T
CS Primary Care Unit, MCP Hahnemann University, Philadelphia, PA, USA.
SO POSTGRADUATE MEDICINE, (1999 Oct 15) 106 (5) 143-8. Ref: 15
Journal code: 0401147. ISSN: 0032-5481.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199911
ED Entered STN: 20000111
Last Updated on STN: 20000111

Entered Medline: 19991124

AB Several chemical agents appear to be useful in primary prevention of CAD and cancer. Randomized trials have found that in specific patient subgroups, tamoxifen and raloxifene decreased the occurrence of breast cancer, and lovastatin and aspirin decreased the frequency of CAD events. Secondary analysis of randomized primary-prevention studies has supported the use of vitamin E and selenium in cancer prevention.

L74 ANSWER 79 OF 135 MEDLINE on STN
AN 1998208873 MEDLINE
DN 98208873 PubMed ID: 9547657
TI Tumor infiltrating lymphocytes in squamous cell carcinoma of the head and neck: mechanisms of enhancement using prostaglandin synthetase inhibitors.
AU Cross D S; Platt J L; Juhn S K; Bach F H; Adams G L
CS Dept. of Otolaryngology/Head and Neck Surgery, University of Minnesota, Minneapolis, USA.
NC HL46810 (NHLBI)
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1997) 400B 1013-24. Ref: 34
Journal code: 0121103. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980609
Last Updated on STN: 19980609
Entered Medline: 19980527

AB Indomethacin has been shown clinically to inhibit growth of SCCHN (Panje, 1981). This inhibition appears to be due to augmentation of cellular immunity. The inhibitory effect of indomethacin may act by limiting tumor associated prostaglandin E2 production, thereby allowing return of costimulatory cytokines by antigen presenting cells. This would have the net result of relief from host unresponsiveness and promotion of B-cell and CTL differentiation, allowing the individual to mount an effective response. The enhancement of tumor infiltrating lymphocytes in SCCHN seen with indomethacin administration could presumably be further augmented when given in combination with cytokine therapy. Future investigation may allow the biochemical staging of an individuals' tumor to determine the optimal combination of cytokine therapy and prostaglandin inhibition through selective use of NSAID's. The effect of NSAID manipulation of prostaglandin and leukotriene metabolism on prevention of metastatic disease in SCCHN has yet to be studied. Given that a preselected, potentially responsive subset of immunocytes exists within the tumor tissue and lymph nodes, the development of the LAK phenomenon in TIL's and tumor draining lymph nodes from surgical specimens is a viable and exceedingly interesting area for future investigations in autologous LAK immunotherapy. The potential exists to harvest a preselected population of tumor infiltrating (Boscia, 1988) or tumor draining immunocytes (McKinnon, 1990). These can then potentially be returned to a state of antigen responsiveness with a combination of cytokine exposure (e.g. rIL-2) and systemic cytokine therapy. With subsequent inhibition of tumor associated prostaglandin synthesis by the systemic administration of prostaglandin synthesis inhibitors, it may be possible to successfully alter the host response to tumor.

L74 ANSWER 80 OF 135 MEDLINE on STN
AN 97221566 MEDLINE
DN 97221566 PubMed ID: 9068612
TI Prostaglandin H synthases, nonsteroidal anti-inflammatory drugs, and colon cancer.
AU Levy G N
CS Department of Pharmacology, University of Michigan, Ann Arbor 48109-0632, USA.
NC CA39018 (NCI)
SO FASEB JOURNAL, (1997 Mar) 11 (4) 234-47. Ref: 109
Journal code: 8804484. ISSN: 0892-6638.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970422
Last Updated on STN: 19970422
Entered Medline: 19970407
AB Members of the structurally diverse class of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs) have the ability to prevent or reduce the occurrence of colorectal, certain other gastrointestinal, and perhaps other cancers. The anticarcinogenic property of NSAIDs has been shown in epidemiological studies with humans and in experimental carcinogenesis studies with animals. In addition, clinical studies of the human disease familial adenomatous polyposis have demonstrated the efficacy of NSAIDs in mediating regression of colorectal adenomas. The mechanism of the anticarcinogenic effect of these drugs is not known, but most hypotheses have involved the common property of the NSAIDs to inhibit prostaglandin synthase (PHS) enzymes and thereby cause a subsequent reduction in levels of prostaglandins (PG) in tissue. Recent reports have questioned the role of PHS inhibition in the anticarcinogenic activity of NSAIDs by showing that some NSAID-related compounds that are not PHS inhibitors can induce the same anticarcinogenic changes in cell cycle and apoptotic response as the PHS inhibitors. In this review we will examine the evidence that NSAIDs are anticarcinogenic, the evidence supporting PHS as the target of NSAIDs, and the evidence for and against inhibition of PG synthesis as the mechanism of cancer prevention by NSAIDs.

L74 ANSWER 81 OF 135 MEDLINE on STN
AN 96239942 MEDLINE
DN 96239942 PubMed ID: 8693304
TI Prevention of gastrointestinal cancer--the potential role of NSAIDs in colorectal cancer.
AU Luk G D
CS Dallas VA Medical Center, University Texas Southwestern Medical Center 75216, USA..
SO SCHWEIZERISCHE MEDIZINISCHE WOCHENSCHRIFT. JOURNAL SUISSE DE MEDECINE, (1996 May 11) 126 (19) 801-12. Ref: 125
Journal code: 0404401. ISSN: 0036-7672.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960823
AB Gastrointestinal cancers are among the leading sites of cancer and leading causes of cancer-related deaths. Gastrointestinal cancers are often at an advanced stage at the time of diagnosis, and are highly resistant to non-surgical therapy. Thus early diagnosis and prevention are approaches that are under active investigation. Screening and surveillance are considered secondary prevention. Primary prevention is the use of dietary or environmental modification or chemopreventive agents. This written review will emphasize the potential role of acetylsalicylic acid and other non-steroidal anti-inflammatory drugs (NSAIDs) in the prevention of gastrointestinal cancer, and specifically colorectal cancer. Cell culture and animal studies have shown that NSAIDs possess anti-proliferative and anti-neoplastic effects. Recent epidemiologic surveys also suggest that individuals who regularly take NSAIDs, particularly acetylsalicylic acid, have about a 50% decrease in colorectal cancer incidence and mortality. However, in the only interventional trial of aspirin (and beta-carotene), a retrospective analysis had inadequate statistical power to demonstrate any protective effect against colorectal cancer. About a dozen small prospective intervention studies have been done in a total of about a hundred patients with familial adenomatous polyposis to test the efficacy of NSAIDs, particularly sulindac. All human trials have shown substantial partial and some complete regression of colorectal and perhaps also duodenal adenomatous polyps. But virtually all patients had regrowth of adenomatous polyps after sulindac was stopped. In addition, sulindac and other NSAIDs result in occasional adverse events such as gastrointestinal bleeding. Thus sulindac cannot be recommended for routine use outside of a study setting. One valid current approach to the prevention of gastrointestinal cancer, and colorectal cancer in particular, is the adoption of a healthy lifestyle and appropriate screening and surveillance. Screening and surveillance guidelines have been developed by several public agencies and their recommendations should be adopted. In addition, we should adopt a healthy lifestyle and diet, which consists of low fat (< 30% to total calories), and high fiber (> 3 daily servings of fruits/vegetables), with the avoidance of red meats (< 3 weekly servings) and alcohol (< 2 drinks daily), and the absolute avoidance of tobacco smoking.

L74 ANSWER 82 OF 135 MEDLINE on STN
AN 93295126 MEDLINE
DN 93295126 PubMed ID: 1305681
TI Piroxicam and other cyclooxygenase inhibitors: potential for cancer chemoprevention.
AU Earnest D L; Hixson L J; Alberts D S
CS Department of Medicine, University of Arizona, Tucson 85724.
NC P01 CA41108 (NCI)
SO JOURNAL OF CELLULAR BIOCHEMISTRY. SUPPLEMENT, (1992) 16I 156-66. Ref: 54
Journal code: 8207539. ISSN: 0733-1959.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199307
ED Entered STN: 19930806
Last Updated on STN: 19930806
Entered Medline: 19930722
AB Piroxicam is a nonsteroidal anti-inflammatory drug (NSAID) widely used for treatment of inflammatory arthritis. Recent experimental and clinical studies suggest that piroxicam, as well as other NSAIDs, may be useful for chemoprevention of colon cancer. While there is less information regarding NSAIDs for chemoprevention of urinary bladder malignancy, there are compelling data which suggest that this should be evaluated. A major effect of NSAIDs is inhibition of cyclooxygenase, the rate-limiting enzyme for conversion of arachidonic acid to important signal molecules, including prostaglandins, which profoundly affect cellular functions in many tissues. The initial enzyme reaction leading to formation of prostaglandin H can be accompanied by cooxidation of xenobiotics resulting in extrahepatic and local tissue production of reactive products which are carcinogenic. The end product prostaglandins, especially prostaglandin E2 (PGE2), are biological modifiers which can significantly affect cell proliferation and tumor growth. High levels of PGE2 stimulate growth of certain tumor cell lines while inhibition of prostaglandin synthesis with indomethacin or piroxicam can cause suppression. The mechanisms for this effect are unclear. Studies in cultured cells exposed to indomethacin show inhibition of G1-to-S phase progression of the cell cycle and a reduction in overall DNA synthesis. It is unclear whether this effect on cell growth results from some direct action of the NSAID or a reduction in prostaglandins or indirectly from modulation of important control signals, such as calcium flux. In addition to cyclooxygenase, NSAIDs can inhibit activity of other enzymes, including phosphodiesterases and cyclic GMP-AMP protein kinases, which may be central to cancer initiation and promotion. NSAIDs can also interfere with transmembrane ion fluxes and with cell-to-cell binding. Prostaglandins can modulate a variety of immunological responses and thereby play an important role in host antitumor immunity. For example, high levels of tissue PGE2 are frequently associated with suppression of immune surveillance and killing of malignant cells. Conversely, immune responses are generally enhanced by drugs that inhibit prostaglandin synthesis. PGE2 can act as a feedback inhibitor for cellular immune processes, such as T-cell proliferation, lymphokine production, and cytotoxicity. This effect is also seen for macrophage activity and natural killer cell toxicity. In general, either increased production of PGE2 or increased sensitivity to normal amounts of PGE2 results in depressed cellular immunity. Cyclooxygenase inhibitors (NSAIDs) such as piroxicam which decrease PGE2 production can stimulate cellular immune function both in vitro and in vivo. A variety of tumor cell lines and human malignancies produce large quantities of prostaglandins.(ABSTRACT TRUNCATED AT 400 WORDS)

L74 ANSWER 83 OF 135 MEDLINE on STN
AN 90349652 MEDLINE
DN 90349652 PubMed ID: 2201035
TI Can oxysterols have some interest in the treatment of tumors?.
AU Beck J P
CS Universite Louis Pasteur, Laboratoire de Recherches en Immunologie, Strasbourg, France.
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, (1990) 348 71-93. Ref: 28

Journal code: 7605701. ISSN: 0361-7742.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199009
ED Entered STN: 19901026
Last Updated on STN: 19970203
Entered Medline: 19900920

L74 ANSWER 84 OF 135 MEDLINE on STN
AN 88303845 MEDLINE
DN 88303845 PubMed ID: 3136454
TI Synthesis of biologically active ether lipids.
AU Mangold H K
CS Institut fur Biochemie und Technologie, H.P.-Kaufmann-Institut, Munster, FRG.
SO PROGRESS IN BIOCHEMICAL PHARMACOLOGY, (1988) 22 1-16. Ref: 84
Journal code: 0036761. ISSN: 0079-6085.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198809
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880909

L74 ANSWER 85 OF 135 MEDLINE on STN
AN 86233497 MEDLINE
DN 86233497 PubMed ID: 3086890
TI Antimetastatic drugs: function and value.
AU Hellmann K
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, (1986) 212 1-16. Ref: 20
Journal code: 7605701. ISSN: 0361-7742.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198607
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860714

L74 ANSWER 86 OF 135 MEDLINE on STN
AN 82282609 MEDLINE
DN 82282609 PubMed ID: 6214207
TI Prostaglandins and the immune response to cancer (review).
AU Ceuppens J; Goodwin J
SO ANTICANCER RESEARCH, (1981) 1 (2) 71-8. Ref: 98
Journal code: 8102988. ISSN: 0250-7005.

CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198210
ED Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19821012

L74 ANSWER 87 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:60324 HCAPLUS
TI Pharmaceutical compositions comprising estetrol derivatives for use in cancer therapy
IN Coelingh, Bennink Herman Jan Tijmen; Bunschoten, Evert Johannes
PA Pantarhei Biosciences B.V., Neth.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004006936	A1	20040122	WO 2003-NL513	20030711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2002-77812 A 20020712
EP 2003-75435 A 20030214

AB The present invention relates to a method of treating or preventing estrogen-sensitive tumors in a mammal, said method comprising the administration of a therapeutically effective amt. of an estrogenic component to said mammal, wherein the estrogenic component is selected from the group consisting of: substances represented by the following formula (I) in which formula R1, R2, R3, R4, independently are a hydrogen atom, a hydroxyl group or an alkoxy group with 1-5 carbon atoms; precursors capable of liberating a substance according to the aforementioned formula when used in the present method; and mixts. of one or more of the aforementioned substances and/or precursors. The estrogenic component according to the invention does not have undesirable proliferative effects on breast and/or endometrial tissue and displays sufficient estrogenicity to prevent that its administration will lead to hypoestrogenism and/or climacteric complaints. Other aspects of the invention relate to pharmaceutical compns., drug delivery systems and kits comprising the aforementioned estrogenic component in combination with an estrogen suppressant.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 88 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007015 HCAPLUS
DN 140:58438
TI Monoclonal anti-MUC1 antibody PAM4 and chimeric antibodies for diagnosis and therapy of pancreatic cancer
IN Gold, David V.; Goldenberg, David M.; Hansen, Hans
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003106497	A1	20031224	WO 2003-GB2585	20030616

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-388313P P 20020614
AB This invention relates to monovalent and multivalent, monospecific antibodies and to monovalent and multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-assocd. antibody designated PAM4. The invention further relates to chimeric PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 89 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007014 HCAPLUS
DN 140:58437
TI Multivalent humanized monoclonal anti-MUC1 antibody PAM4 for diagnosis and treatment of cancer
IN Goldenberg, David M.; Hansen, Hans; Qu, Zhengxing
PA Immunomedics, Inc., USA; McCall, John Douglas
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2003106495 A2 20031224 WO 2003-GB2593 20030616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-388314P P 20020614
AB This invention relates to monovalent and multivalent, monospecific antibodies and to multivalent, multispecific antibodies. One embodiment of these antibodies has one or more identical binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these antibodies has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional antibodies in a host. More specifically, the present invention relates to the tumor-assocd. antibody designated PAM4. The invention further relates to humanized and human PAM4 antibodies, and the use of such antibodies in diagnosis and therapy.

L74 ANSWER 90 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:931165 HCAPLUS
DN 139:391341
TI Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
IN Zeldis, Jerome B.
PA Celgene Corporation, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003097040	A1	20031127	WO 2003-US15468	20030516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-380842P P 20020517
US 2002-424601P P 20021106
OS MARPAT 139:391341
AB Methods of treating, preventing and/or managing cancer as well as and

diseases and disorders assocd. with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects assocd. with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 91 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:777523 HCAPLUS
DN 139:307756
TI 4,5-Dihydro-1H-pyrazole derivatives useful as mitotic kinesin inhibitors, and their pharmaceutical compositions and use in the treatment of cancer
IN Breslin, Michael J.; Coleman, Paul J.; Cox, Christopher D.; Culberson, J. Christopher; Hartman, George D.; Mariano, Brenda J.; Torrent, Maricel
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003079973	A2	20031002	WO 2003-US6403	20030304

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-362922P P 20020308
OS MARPAT 139:307756
AB The invention relates to dihydropyrazole compds. that are useful for treating cellular proliferative diseases, for treating disorders assocd. with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also related to compns. which comprise these compds., and methods of using them to treat cancer in mammals. The compds. are disclosed as pyrazole derivs. I [R1 = various (un)substituted acyl and thioacyl, sulfonyl, alkyl, (hetero)aryl, etc.; R2 = (un)substituted alk(en/yn)yl, aryl, perfluoroalkyl, (hetero)aralkyl, cycloalkyl, or heterocyclyl; R3, R4, R5, R6 = H, (un)substituted alk(en/yn)yl, cycloalkyl, (hetero)aralkyl, or heterocyclyl; or R3R4 or R5R6 (when W and Z are bonds) = atoms to form (CH2)1-5 with one optional replacement of a CH2 by O, S, SO, SO2, NHCO or NH or derivs.; Y, W, Z = bond, CO, C:S, S, SO, SO2, CH(OH), or O] and their pharmaceutically acceptable salts or stereoisomers. Approx. 65 compds. I are prepd. and claimed by name, and another 150 compds. are claimed. For instance, 2,5-difluoroacetophenone was lithiated and coupled with 3-(benzyloxy)benzaldehyde, followed by dehydration with

trifluoroacetic anhydride, to give chalcone deriv. II. This compd. was debenzylated with BBr3, then cyclized with hydrazine and acetylated in situ with AcOH, to give title compd. III. In a kinesin ATPase in vitro assay, using human KSP motor domain construct and microtubules from bovine brain tubulin, the example compds. had IC50 .ltoreq. 50 .mu.M.

L74 ANSWER 92 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719518 HCAPLUS
DN 139:259962
TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of cancer
IN Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.
PA Immunomedics, Inc., USA; Mccall, John Douglas
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003074566	A2	20030912	WO 2003-GB885	20030303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004001825	A1	20040101	US 2003-377121	20030303
PRAI US 2002-360229P	P	20020301		

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-assocd. antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L74 ANSWER 93 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:590931 HCAPLUS
DN 139:111643
TI Anti-cancer combination and use thereof
IN Ben-sasson, Shmuel A.; Tsirulnikov, Lilia; Vainstein, Vladimir
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Children's Medical Center Corporation
SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003061566	A2	20030731	WO 2002-US41767	20021231

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-351946P P 20020124

AB The present invention relates to the surprising discovery that the combination of several agents, each well known for its established role in treating cancer, inflammation, hemostasis, bone resorption or serving as a solubilizing vehicle, results in a synergistic anti-cancer compn. Furthermore, the combination of at least three agents allows the cytotoxic agent, such as cyclophosphamide, to be used at a lower dosage than when administered alone. One predicted consequence of this treatment, therefore, is a highly desirable redn. in toxic side effects due to the cytotoxic agent.

L74 ANSWER 94 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:472516 HCAPLUS
DN 139:53031
TI Preparation of furopyrimidinones as mitotic kinesin inhibitors for treatment of cancer
IN Fraley, Mark E.; Hartman, George D.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003050122	A2	20030619	WO 2002-US38487	20021202
WO 2003050122	A3	20031204		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-338380P P 20011206
OS MARPAT 139:53031

AB Syntheses for title compds. I [wherein one of W, Y, or Z = O and the other 2 = CH; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl, CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] as KSP kinesin inhibitors are given (no data). For example, a detailed synthesis for the prepn. of II is outlined. The scheme involves the reaction of tert-Bu 2-furylcarbamate with CO2 and benzylamine in the presence of t-BuLi, substitution with butyryl chloride, cyclization, bromination, addn. of N,N-dimethylethylenediamine, and coupling with 4-bromobenzoyl chloride. I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases assocd. with KSP kinesin activity, such as cancer (no data).

L74 ANSWER 95 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:472471 HCAPLUS
DN 139:69276
TI Preparation of thienopyrimidines as mitotic kinesin inhibitors for the treatment of cancer
IN Fraley, Mark E.; Hartman, George D.; Hoffman, William F.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003050064	A2	20030619	WO 2002-US38417	20021202
	WO 2003050064	A3	20031016		
	WO 2003050064	B1	20031218		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-338383P P 20011206
OS MARPAT 139:69276
AB Title compds. I [wherein one of W, Y, or Z = S and the other 2 = CH; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl,

aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl, CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting KSP kinesin. For example, amidation of Me 3-aminothiophene-2-carboxylate with butyryl chloride afforded Me 3-(butyrylamino)thiophene-2-carboxylate, which was sapond. to give the acid. Amidation with benzylamine, followed by cyclization provided 3-benzyl-2-propylthieno[3,2-d]pyrimidin-4(3H)-one. Bromination, coupling with N,N-dimethylethylenediamine, and reaction with 4-bromobenzoyl chloride gave the N-[1-(thienopyrimidinyl)propyl]benzamide II. The latter inhibited human poly-histidine tagged KSP motor domain with an IC50 value of .ltoreq.50 .mu.M. Thus, I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases assocd. with KSP kinesin activity, such as cancer (no data). Prepn. of thienopyrimidine kinesin inhibitors from thiophenes, amines, and acid chlorides.

L74 ANSWER 96 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:472337 HCAPLUS
DN 139:69275
TI Preparation of thiazolopyrimidinones as mitotic kinesin inhibitors for treatment of cancer
IN Fraley, Mark E.; Hartman, George D.; Hoffman, William F.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003049679	A2	20030619	WO 2002-US38313	20021202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-338344P P 20011206
OS MARPAT 139:69275
AB Syntheses for title azolopyrimidinone compds. I [wherein Y = CH or N; W = CH, S, or O; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl,

alkenyl, alkynyl, aralkyl, aryl, or heterocyclyl; R2, R2', R3, and R3' = independently H, perfluoroalkyl, CO2H, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)cyclyl; or NR3R3' = (un)substituted heterocyclyl; R4 = independently halo, OH, CN, perfluoroalkyl(oxy), CO2H, (CO)aNR7R8, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl,(CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted CO-Ob-(cyclo)alkyl, CO-Ob-aryl, CO-Ob-heterocyclyl, (cyclo)alkyl, alkenyl, alkynyl, aryl, or heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl, aryl, or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] as KSP kinesin inhibitors are given (no data). For example, a detailed synthesis for the prepn. of II is outlined (no data). The reaction scheme involves the cyclization of Et 5-amino-1,3-thiazole-4-carboxylate with tri-Me orthobutyrate and benzylamine to afford the [1,3]thiazolo[5,4-d]pyrimidin-7(6H)-one intermediate, followed by bromination, amination with N,N-dimethylethylenediamine, and amidation with 4-bromobenzoyl chloride. I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases assocd. with KSP kinesin activity, such as cancer (no data).

L74 ANSWER 97 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:472336 HCAPLUS
DN 139:53029
TI Preparation of cyclopenta[d]pyrimidinones as mitotic kinesin inhibitors for the treatment of cancer
IN Fraley, Mark E.; Garbaccio, Robert M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003049678	A2	20030619	WO 2002-US38312	20021202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-338379P P 20011206
OS MARPAT 139:53029
AB Title compds. I [wherein one of R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' =

(un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl, CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; m = 0-3; n = 1-3; and pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting KSP kinesin. For example, reaction of Et 2-aminocyclopentenecarboxylate with 1,1,1-trimethoxybutane and benzylamine gave 3-benzyl-2-propyl-3,5,6,7-tetrahydro-4H-cyclopenta[d]pyrimidin-4-one. Bromination, substitution with N,N-dimethylethylenediamine, and coupling with 4-bromobenzoyl chloride provided II. The latter inhibited human poly-histidine tagged KSP motor domain with an IC50 value of .ltoreq.50 .mu.M. Thus, I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases assocd. with KSP kinesin activity, such as cancer.

L74 ANSWER 98 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:376563 HCAPLUS
DN 138:385439
TI Preparation of quinazolinone mitotic kinesin inhibitors for treating cancer
IN Fraley, Mark E.; Hoffman, William F.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003039460	A2	20030515	WO 2002-US35111	20021101
	WO 2003039460	A3	20030731		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-344453P P 20011107
OS MARPAT 138:385439
AB The present invention relates to quinazolinones (shown as I; variables defined below; e.g. 3-benzyl-2-[1-(4-methylpiperazin-1-yl)propyl]quinazolin-4(3H)-one) that are useful for treating cellular proliferative diseases, for treating disorders assocd. with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also related to compns. which comprise these compds., and methods of using them to treat cancer in mammals. Twelve examples of I were found in a kinesin ATPase in vitro assay to have IC50 .ltoreq.50 .mu.M. Although the methods of prepn.

are not claimed, 1 example prepn. of I and characterization data for another 10 examples of I are included. For I: NR = 5-12 membered N-contg. heterocycle, which is optionally substituted with 1-6 R5 groups and which optionally incorporates 1-2 addnl. heteroatoms = N, O and S in the heterocycle; a = 0, 1; b = 0, 1; m = 0-2; n = 0-4; R1 = H, C1-C10 alkyl, aryl, C2-C10 alkenyl, C2-C10 alkynyl, C1-C6 perfluoroalkyl, C3-C8 cycloalkyl, and heterocyclyl. R2 and R3 = H, (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, C1-C6 perfluoroalkyl, (C:O)aObC3-C8 cycloalkyl, (C:O)aObheterocyclyl, SO2NR7R8, and SO2C1-C10 alkyl; R4 = (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, halo, OH, ObC1-C6 perfluoroalkyl, (C:O)aNR7R8, CN, (C:O)aObC3-C8 cycloalkyl, (C:O)aObheterocyclyl, SO2NR7R8, and SO2C1-C10 alkyl; R5 is (C:O)aObC1-C10 alkyl, (C:O)aObaryl, C2-C10 alkenyl, C2-C10 alkynyl, (C:O)aOb heterocyclyl, CO2H, halo, CN, OH, ObC1-C6 perfluoroalkyl, Oa(C:O)bNR7R8, oxo, CHO, N(O)R7R8, or C(O)aObC3-C8 cycloalkyl; addnl. details are given in the claims.

L74 ANSWER 99 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:356569 HCAPLUS
DN 138:367591
TI Anti-TRAIL receptor antibodies and other therapeutic agents for treating neoplastic, inflammatory and autoimmune diseases
IN Zhou, Tong; Ichikawa, Kimihisa; Kimberly, Robert P.; Koopman, William J.; Oshumi, Jun; Lobuglio, Albert F.; Buchsbaum, Donald J.
PA UAB Research Foundation, USA
SO PCT Int. Appl., 274 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003038043	A2	20030508	WO 2002-US34420	20021025
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003133932	A1	20030717	US 2002-281479	20021025
PRAI	US 2001-346402P	P	20011101		
	US 2002-391478P	P	20020624		

AB An antibody of the invention interacts with tumor necrosis factor-related apoptosis-inducing ligand receptor such as human DR5 or DR4 to produce agonistic or antagonistic effects downstream of the receptor including inhibition of cell proliferation and apoptosis. Methods and uses for the antibodies, optionally in combination with various therapeutic agents, are detailed, including treatment of apoptosis-related disease and treatment of dysregulated cell growth, such as cancer, inflammation and autoimmune diseases.

L74 ANSWER 100 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:335080 HCAPLUS
DN 138:337982
TI Preparation of 2-carboxamidopyrroles as tyrosine kinase inhibitors
IN Trotter, B. Wesley
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003035619	A1	20030501	WO 2002-US33962	20021023
WO 2003035619	C1	20030703		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-343000P P 20011025
OS MARPAT 138:337982
AB Title compds. I [wherein V = (cyclo)alkyl, aryl, heterocyclyl, or CO; W = a bond, cycloalkyl, aryl, or heterocyclyl; Ra and Rb = independently H, OR7, or (un)substituted alkyl, aryl, or heterocyclyl; R1 = independently H, halo, OR7, COR7, CO2R7, CON(R7)2, N(R7)2, SO2N(R5)2, or (un)substituted (cyclo)alkyl, aryl, or heterocyclyl; R2 = CO2R7, (CRb2)N(R7)2, (CRb2)nOR7, CON(R7)2, CONR7OR7, CONH(CRb2)qR7, CONR7NHCOR7, CONR7SO2OR7, CONH(CRb2)qCON(R7)2, or (un)substituted alkyl or aryl; R3 = H or (un)substituted alkyl, aralkyl, aryl, or heterocyclyl(alkyl); R4 = H, halo, OR7, COR7, CO2R7, CON(R7)2, N(R7)2, SO2N(R5)2, or (un)substituted (cyclo)alkyl, aryl, or heterocyclyl; R5 = independently H, or (un)substituted alkyl, aryl, or heterocyclyl; R6 = independently H, OR7, or (un)substituted alkyl, aralkyl, aryl, or heterocyclyl(alkyl); R7 = independently H or (un)substituted alkyl, aralkyl, aryl, or heterocyclyl(alkyl); n = independently 0-6; q = 0-5; or pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting, modulating, and/or regulating signal transduction of both receptor type and non-receptor type tyrosine kinases. For example, N-[[5-(tert-butoxycarbonyl)-3-(ethoxycarbonyl)-4-ethyl-1H-pyrrol-2-yl]methyl]-4-methoxybenzenaminium trifluoroacetate was converted to the acid using TFA (no data), and the product amidated with propylamine to give II.bul.TFA. Compds. of the invention inhibited insulin-like growth factor I (IGF-1R) or insulin receptor (IR) kinase activity with IC50 .ltoreq. 100 .mu.M. Thus, I are useful for the treatment of protein kinase related disorders, such as cancer, diabetes, autoimmune disorders, hyperproliferation disorders, aging, acromegaly, and Crohn's disease (no data).
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 101 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:335077 HCAPLUS
DN 138:337981
TI Preparation of pyrroles as tyrosine kinase inhibitors
IN Trotter, B. Wesley; Bell, Ian M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003035616	A2	20030501	WO 2002-US33921	20021021
	WO 2003035616	A3	20031023		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-342900P P 20011025
OS MARPAT 138:337981
AB Title compds. I [wherein X = O or NRb; Ra = H, (un)substituted alkyl, or OR6; Rb = H or (un)substituted alkyl; R1 = H, OR6, N(R6)2, or (un)substituted (cyclo)alkyl, aryl, or heterocyclyl; R2 = H, CO2R6, COR6, (CRa2)nN(R6)2, CON(R6)2, NR6COR6, (CRa2)nOR6, CONR6CONHR6, CONR6SO2R6, CONR6OR6, or (un)substituted alkyl, aryl, heterocyclyl, or aralkyl; R3 = CO2R6, COR6, (CRa2)nN(R6)2, (CRa2)nOR6, CON(R6)2, NR6COR6, or (un)substituted alkyl, aralkyl, heterocyclyl, or aryl; R4 = H or (un)substituted alkyl; R6 = H or (un)substituted alkyl, aryl, aralkyl, or heterocyclyl(alkyl); n = 0-6; and pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting, modulating, and/or regulating signal transduction of both receptor type and non-receptor type tyrosine kinases. For example, addn. of PhCH2COCl to Meldrum's acid and subsequent treatment with t-BuOH gave tert-Bu 3-oxo-4-phenylbutanoate (no data). Cyclization of tert-Bu 3-oxo-4-phenylbutanoate , NaNO2, and Et 3-oxobutanoate in the presence of Zn and NH4OAc, followed by oxidn. provided II. Compds. of the invention inhibited insulin-like growth factor I (IGF-1R) or insulin receptor (IR) kinase activity with IC50 .ltoreq. 100 .mu.M. Thus, I are useful for the treatment of protein kinase related disorders, such as cancer, diabetes, autoimmune disorders, hyperproliferation disorders, aging, acromegaly, and Crohn's disease (no data).

L74 ANSWER 102 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:335076 HCAPLUS
DN 138:353831
TI Preparation of 2-carboxypyrroles as tyrosine kinase inhibitors
IN Trotter, B. Wesley; Bell, Ian M.; Zartman, C. Blair; Lindsley, Craig; Zhao, Zhijian
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 208 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003035615	A2	20030501	WO 2002-US33920	20021021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-343119P P 20011025
OS MARPAT 138:353831
AB Title compds. I [wherein V = (cyclo)alkyl, aryl, heterocyclyl, or CO; Ra and Rb = independently H, OR7, or (un)substituted alkyl, aryl, or heterocyclyl; R1 = independently H, halo, OR7, COR7, CO2R7, CON(R6)2, N(R7)2, SO2N(R5)2, or (un)substituted (cyclo)alkyl, aryl, or heterocyclyl; R2 = CO2R7, (CRb2)nN(R7)2, CON(R7)2, CONR7OR7, CONH(CRb2)qR7, CONR7NHCOR7, CONR7SO2OR7, (CRb2)nOR7, CONH(CRb2)qCON(R7)2, or (un)substituted alkyl or aryl; R3 and R7 = independently H or (un)substituted alkyl, aralkyl, aryl, or heterocyclyl(alkyl); R4 = (un)substituted alkyl, aryl, aralkyl, or heterocyclyl; R5 = independently H or (un)substituted alkyl, aryl, or heterocyclyl; R6 = independently H, OR7, or (un)substituted alkyl, aralkyl, aryl, or heterocyclyl(alkyl); m = 0-6; n = 0-6; p = 0-6; q = 0-5; and pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting, modulating, and/or regulating signal transduction of both receptor type and non-receptor type tyrosine kinases. For example, addn. of PhCH2COCl to Meldrum's acid and subsequent treatment with t-BuOH gave tert-Bu 3-oxo-4-phenylbutanoate (no data). Cyclization with NaNO2 and Et 3-oxobutanoate in the presence of Zn and NH4OAc, followed by oxidn. and reductive addn. of 4-chloroaniline provided II. Compds. of the invention inhibited insulin-like growth factor I receptor (IGF-1R) or insulin receptor (IR) kinase activity with IC50 values of .ltoreq.100 .mu.M. Thus, I are useful for the treatment of protein kinase related disorders, such as cancer, diabetes, autoimmune disorders, hyperproliferation disorders, aging, acromegaly, and Crohn's disease (no data).

L74 ANSWER 103 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:335075 HCAPLUS
DN 138:337980
TI Preparation of 2-carboxy-5-formylpyrroles as tyrosine kinase inhibitors
IN Trotter, B. Wesley; Bell, Ian M.; Zartman, C. Blair
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2003035614	A2	20030501	WO 2002-US33919	20021021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-342902P P 20011025

OS MARPAT 138:337980

AB Title compds. I [wherein R1 = H or CO2R2; R2, R3, and R4 = independently H or (un)substituted alkyl, aryl, aralkyl, or heterocyclyl(alkyl); with the proviso that R4 .noteq. Bu-t; R5 = H or (un)substituted alkyl; or pharmaceutically acceptable salts or stereoisomers thereof] were prepd. for inhibiting, modulating, and/or regulating signal transduction of both receptor type and non-receptor type tyrosine kinases. For example, cyclization of Et 3-oxobutanoate, NaNO2, and tert-Bu 3-oxobutanoate in the presence of NH4OAc and Zn in AcOH to the pyrrole (no data), followed by oxidn. gave II. Compds. of the invention inhibited insulin-like growth factor I (IGF-1R) or insulin receptor (IR) kinase activity with IC50 .ltoreq. 100 .mu.M. Thus, I are useful for the treatment of protein kinase related disorders, such as cancer, diabetes, autoimmune disorders, hyperproliferation disorders, aging, acromegaly, and Crohn's disease (no data).

L74 ANSWER 104 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:282319 HCAPLUS

DN 138:302654

TI Interleukin-21 receptor agonists and antagonists for treating transplant rejection, autoimmune diseases, cancers and infections

IN Carter, Laura; Whitters, Matthew J.; Collins, Mary; Young, Deborah A.; Larsen, Glenn; Donaldson, Debra D.; Lowe, Leslie D.; Dunussi, Kyri; Ma, Margery; Witek, Joann S.; Kasaian, Marion T.; Ungar, Michelle

PA Wyeth, John, and Brother Ltd., USA

SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003028630	A2	20030410	WO 2002-US29839	20021004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG

	US 2003049798	A1	20030313	US 2001-972218	20011004
	US 2004016010	A1	20040122	US 2003-418450	20030417
PRAI	US 2001-972218	A	20011004		
	US 2002-373746P	P	20020417		
	US 1998-40005	A1	19980317		
	US 2000-560766	B2	20000428		
	US 2000-569384	A2	20000511		

AB Methods and compns. for modulating interleukin-21 (IL-21)/IL-21 receptor (MU-1) activity using agonists or antagonists of IL-21 or IL-21 receptor ('IL-21R' or 'MU-1'), are disclosed. IL-21/IL-21R antagonists can be used to induce immune suppression in vivo, e.g., for treating or preventing immune cell-assocd. pathologies (e.g., pathologies assocd. with aberrant activity of one or more of mature T cells (mature CD8+, mature CD4+ T cells), mature NK cells, B cells, macrophages and megakaryocytes, including transplant rejection and autoimmune disorders). IL-21/IL-21R agonists can be used by themselves or in combination with an antigen, e.g., as an adjuvant (e.g., a vaccine adjuvant), to up-regulate an immune response in vivo, e.g., for example, for use in treating cancer and infectious disorders.

L74 ANSWER 105 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:261660 HCAPLUS
DN 138:286028
TI STAT-modulating N-acyl homoserine lactones for treating cancers, lipid metabolic disorders and immune diseases
IN Shaw, Peter; Pritchard, Davi; Li, Li
PA University of Nottingham, UK
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003026641	A2	20030403	WO 2002-GB4232	20020917
	WO 2003026641	A3	20030612		
	WO 2003026641	C1	20030717		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-22914 A 20010922
OS MARPAT 138:286028
AB The use of a compd. selected from a range of compds. including quorum sensing mols., N-acyl homo serine lactones, N-(3-oxododecanoyl)-L-homoserine lactone, inhibitors to modulate STAT activity for the treatment of a range of diseases including cancer, breast cancer, obesity, lipid metab. disorders, immune disease, immune deficiency or immune disorders. The range of compds. also include JAK, ErbB1, EGF, ErbB1 inhibitors, EGF

inhibitors, STAT inhibitors, IL-13, IL-13E13K, sulpher methoxyzol, ubiquitin E3 ligase, serine phosphatase, tyrosine phosphatase, SOCs, Pias proteins, STAT1 inhibitors, STAT2 inhibitors, STAT3 inhibitors, STAT4 inhibitors, STAT5 inhibitors, STAT6 inhibitors, etc.

L74 ANSWER 106 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:202621 HCAPLUS
DN 138:238027
TI Preparation of 3-(2-indolyl)quinolin-2(1H)-ones as tyrosine kinase inhibitors
IN Peckham, Jennifer P.; Hoffman, William F.; Arrington, Kenneth L.; Fraley, Mark E.; Hartman, George D.; Kim, Yuntae; Hanney, Barbara; Spencer, Keith L.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003020699	A2	20030313	WO 2002-US27114	20020826
WO 2003020699	A3	20030522		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-316123P P 20010830
AB Title compds., including I (R groups undefined), were prepd. and inhibitors, regulators, and/or modulators of tyrosine kinase signal transduction. For example, 1-(tert-butoxycarbonyl)-5-[(tert-butyldimethylsilyl)oxy]-1H-indol-2-ylboronic acid was coupled with 2-chloro-3-iodoquinoline (prepn. of starting materials given) in the presence of Pd(PPh3)4 and K3PO4 in dioxane to give the protected 3-(2-indolyl)quinoline deriv. Deprotection using triethylamine trihydrofluoride afforded the alc. Reaction with 1-(2-chloroethyl)piperidine.bul.HCl and Cs2CO3 in DMF followed by reflux at 110.degree. in AcOH and H2O for 12 h provided II. Compds. of the invention inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 .mu.M - 5.0 .mu.M. Thus, I and compns. contg. I are useful for the treatment of tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

L74 ANSWER 107 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:117808 HCAPLUS
DN 138:170248
TI Preparation of 4-(thiazolyl)-2-pyrimidinamines as tyrosine kinase

inhibitors
IN Fraley, Mark E.; Hoffman, William F.; Hartman, George D.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011838	A1	20030213	WO 2002-US23882	20020727

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-309407P P 20010801
OS MARPAT 138:170248
AB The present invention relates to title compds. I [wherein R1a = H, (un)substituted alkyl, OR8, or N(R8)2; R1 and R2 = independently H, halo, CF3, (CH2)tR9COR8, COR9, (CH2)tOR8, CN, (CH2)tNR7R8, (CH2)CONR7R8, CO2R8, (CH2)tSO0-2(CH2)tNR7R8, or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkenyl, or alkynyl; R3 = H, CN, halo, N(R8)2, OR8, or (un)substituted (ar)alkyl or aryl; R7 = H or (un)substituted (ar)alkyl; R8 = independently H or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or aralkyl; or NR7R8 = (un)substituted heterocyclyl; R9 = independently (un)substituted alkyl, heterocyclyl, or aryl; W = aryl or heterocyclyl; m = 0-2; n = independently 0-6; p = 0-4; t = independently 0-6; or pharmaceutically acceptable salts, hydrates, or stereoisomers thereof], which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, cyclization of 2-bromo-1-[2-(methylthio)pyrimidin-4-yl]ethanone (3-step prepn. given) with thiourea in EtOH gave 5-bromo-4-[2-(methylthio)pyrimidin-4-yl]-1,3-thiazol-2-amine.bul.HBr. Oxidn. to the methylsulfinyl deriv. using oxone followed by substitution with 3,5-dimethylaniline afforded II. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC values between 0.01 M and 5.0 M. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age relate80d macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 108 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:117807 HCAPLUS
DN 138:153548
TI Preparation of 4-(pyrazolyl)-2-pyrimidinamines as tyrosine kinase inhibitors
IN Fraley, Mark E.; Peckham, Jennifer P.; Arrington, Kenneth L.; Hoffman, William F.; Hartman, George D.

PA Merck & Co., Inc., USA
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011837	A1	20030213	WO 2002-US23879	20020726

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-309399P P 20010801
OS MARPAT 138:153548
AB The present invention relates to title compds. I [wherein R1a = H, (un)substituted alkyl, OR8, or N(R8)2; R1 and R2 = independently H, halo, CF3, (CH2)tR9COR8, COR9, (CH2)tOR8, CN, (CH2)tNR7R8, (CH2)tCONR7R8, CO2R8, (CH2)tSO0-2(CH2)tNR7R8, or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkenyl, or alkynyl; R3 = independently H, CN, halo, N(R3)2, (CH2)tOR8, or (un)substituted (ar)alkyl or aryl; R7 = independently H or (un)substituted (ar)alkyl; R8 = independently H or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or aralkyl; or NR7R8 = (un)substituted heterocyclyl; R9 = independently (un)substituted heterocyclyl, alkyl, or aryl; V = a bond, aryl, or heterocyclyl; W = aryl or heterocyclyl; m = 0-2; n = 0-6; p = 0-4; t = independently 0-6; and pharmaceutically acceptable salts, hydrates, and stereoisomers thereof], which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, 2-(methylthio)pyrimidine-4-carboxylic acid was amidated with dimethylhydroxylamine.bul.HCl in the presence of EDC and TEA, and the product treated with MeMgBr in Et2O to give 1-[2-(methylthio)pyrimidin-4-yl]ethanone. Coupling with N,N-dimethylformamide dimethylacetal followed by cyclization with phenylhydrazine afforded 2-(methylthio)-4-(1-phenyl-1H-pyrazol-3/5-yl)pyrimidine. Oxidn. with oxone and reaction with 3-chloroaniline provided the 4-(pyrazolyl)-2-pyrimidinamine II. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 .mu.M and 5.0 .mu.M. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 109 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007835 HCAPLUS
DN 140:58443
TI Antibodies, fragments and peptibodies specific to human angiopoietin-2 for treating inflammatory diseases and cancers
IN Oliner, Jonathan Daniel; Min, Hosung

PA Amgen Inc., USA
SO U.S. Pat. Appl. Publ., 191 pp., Cont.-in-part of U.S. Pat. Appl. 2003 229,023.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003236193	A1	20031225	US 2003-410998	20030409
	US 2003229023	A1	20031211	US 2002-269695	20021010
PRAI	US 2001-328624P	P	20011011		
	US 2002-414155P	P	20020927		
	US 2002-269695	A2	20021010		

AB Disclosed are angiopoietin-2-specific antibodies or binding peptides. Also disclosed are peptibodies comprising the peptides, methods of making such peptides and peptibodies, and methods of treatment using such peptides and peptibodies for inflammatory diseases. The angiopoietin 2-specific binding peptides may also be used in combination with an anti-inflammatory agent or a DMARD, SAARD or NSAID, such as methotrexate, TNF inhibitor, IL-1 inhibitor, TACE inhibitor, COX-2 inhibitor, and P-38 inhibitor.

L74 ANSWER 110 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:817913 HCAPLUS
DN 139:322280
TI Human monoclonal antibodies to epidermal growth factor receptor for diagnosis and treatment of cancers and autoimmune diseases
IN Van de Winkel, Jan G. J.; Van Dijk, Marcus A.; Halk, Edward; Gerritsen, Arnout F.; Petersen, Jorgen; Baadsgaard, Ole
PA Genmab, Inc., Den.
SO U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 172,317.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003194403	A1	20031016	US 2002-320094	20021216
	US 2003091561	A1	20030515	US 2002-172317	20020613
PRAI	US 2001-298172P	P	20010613		
	US 2002-172317	A2	20020613		

AB Isolated human monoclonal antibodies which specifically bind to human EGFR, and related antibody-based compns. and mols., are disclosed. The human antibodies can be produced by a transfectoma or in a non-human transgenic animal, e.g., a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V-D-J recombination and isotype switching. Also disclosed are pharmaceutical compns. comprising the human antibodies, non-human transgenic animals and hybridomas which produce the human antibodies, and therapeutic and diagnostic methods for using the human antibodies.

L74 ANSWER 111 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:492716 HCAPLUS
DN 139:63316
TI Methods using a combination of a 3-heteroaryl-2-indolinone and a cyclooxygenase-2 inhibitor for the treatment of neoplasia

IN Masferrer, Jaime L.; Cherrington, Julie M.; Leahy, Kathleen M.; Zweifel, Ben S.
PA Pharmacia Corporation, USA
SO U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of Appl. No. PCT/US99/30693. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 17

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003119895	A1	20030626	US 2002-150546	20020516
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2003097044	A1	20031127	WO 2003-US15582	20030515

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-113786P	P	19981223	
WO 1999-US30693	A2	19991222	
US 2002-150546	A	20020516	

OS MARPAT 139:63316
AB The invention provides methods and compns. useful for treatment or prevention of neoplasia by administering a combination comprising a 3-heteroaryl-2-indolinone compd. (prepn. included) and a COX-2 selective inhibitor. Further provided are compns., pharmaceutical compns., and kits for treatment and prevention of neoplasia.

L74 ANSWER 112 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:454829 HCAPLUS
DN 139:35100
TI Methods and compositions for modulating interleukin-21 (IL-21) or IL-21 receptor (IL-21R) activity and therapeutic uses
IN Carter, Laura; Carreno, Beatriz; Lowe, Leslie D.; Whitters, Matthew J.; Dunussi, Kyri; Collins, Mary; Ma, Margery; Young, Deborah A.; Witek, Joann S.; Larsen, Glenn; Kasaian, Marion T.; Donaldson, Debra D.; Unger, Michelle
PA Wyeth, John, and Brother Ltd., USA
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. Ser. No. 972,218. CODEN: USXXCO
DT Patent

LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003108549	A1	20030612	US 2002-264634	20021004
	US 6057128	A	20000502	US 1998-40005	19980317
	US 2003049798	A1	20030313	US 2001-972218	20011004
	US 2004016010	A1	20040122	US 2003-418450	20030417
PRAI	US 1998-40005	A1	19980317		
	US 2000-560766	B2	20000428		
	US 2000-569384	A2	20000511		
	US 2001-972218	A2	20011004		
	US 2002-373746P	P	20020417		

AB Methods and compns. for modulating interleukin-21 (IL-21)/IL-21 receptor activity using agonists or antagonists of IL-21 or IL-21 receptor (IL-21R or MU-1), are disclosed. IL-21/IL-21R antagonists can be used to induce immune suppression in vivo, e.g., for treating or preventing immune cell-assocd. pathologies (e.g., pathologies assocd. with aberrant activity of one or more of mature T cells (mature CD8+, mature CD4+ T cells), mature NK cells, B cells, macrophages and megakaryocytes, including transplant rejection and autoimmune disorders). IL-21/IL-21R agonists can be used by themselves or in combination with an antigen, e.g., as an adjuvant (e.g., a vaccine adjuvant), to up-regulate an immune response in vivo, e.g., for example, for use in treating cancer and infectious disorders.

L74 ANSWER 113 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:810109 HCAPLUS
DN 139:271044
TI Anti-cancer activity of carvedilol and its isomers
IN Burman, Anand C.; Mukherjee, Rama; Jaggi, Manu; Singh, Anu T.
PA Dabur Research Foundation, India
SO U.S., 14 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6632832	B1	20031014	US 2002-238992	20020910
PRAI	US 2002-238992		20020910		

AB The present invention provides for pharmaceutical compns. comprising carvedilol for treatment of cancer. More particularly the invention relates to the use of carvedilol for treatment of cancers of the colon, ovary, breast, prostate, pancreas, lung, melanoma, glioblastoma, oral cancer and leukemias. Although not bound to any theory, the anticancer activity of carvedilol appears to be attributed to the inhibition of Epidermal Growth Factor and Platelet derived growth factor dependent proliferation of cancer cells. Further, carvedilol exerts anticancer effect by inhibition of the Protein kinase C (PKC) activity and that of the cyclooxygenase 2 enzyme. The invention also relates to the anticancer activity of the optically pure isomers S(-) and R(+) of carvedilol and the use of carvedilol and its isomers in pharmaceutical compns. for the treatment of cancer.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 114 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:580960 HCAPLUS
DN 139:206969
TI The statins: multifunctional antithrombotic and antineoplastic drugs
AU Splichal, James E.; Stamm, Jason A.; Ornstein, Deborah L.
CS Department of Hematology and Oncology, Lackland Air Force Base, Wilford Hall Medical Center, San Antonio, TX, USA
SO Seminars in Thrombosis and Hemostasis (2003), 29(3), 259-274
CODEN: STHMBV; ISSN: 0094-6176
PB Thieme Medical Publishers, Inc.
DT Journal; **General Review**
LA English
AB A review. Statins are approved by the Food and Drug Administration (FDA) for the treatment of hypercholesterolemia and have shown remarkable activity in preventing cardiovascular morbidity and mortality. The versatility of statins is increasingly being appreciated, however, and lowering cholesterol is only one attribute among many shared by this class of drugs. Most statins appear to have antithrombotic activity that is unrelated to the ability to reduce cholesterol levels, and several have significant antitumor effects. This article reviews the lab. and clin. evidence that statins have antithrombotic and anticancer activity, discusses the ways in which these two activities intersect, and proposes novel uses for statins for the treatment of conditions other than hypercholesterolemia.
RE.CNT 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 115 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:536141 HCAPLUS
DN 139:206926
TI Nonsteroidal anti-inflammatory and cyclooxygenase-2-selective inhibitors in clinical cancer prevention trials
AU Hawk, Ernest T.; Viner, Jaye L.; Umar, Asad
CS Gastrointestinal & Other Cancers Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda, MD, USA
SO Progress in Experimental Tumor Research (2003), 37(COX-2), 210-242
CODEN: PEXTAR; ISSN: 0079-6263
PB S. Karger AG
DT Journal; General Review
LA English
AB A review, which presents published data on the title compds. that have been tested in cancer-prevention trials, highlights ongoing research, and considers the public-health impact this class of compds. may have on cancer and other common chronic diseases of aging.
RE.CNT 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 116 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:407305 HCAPLUS
DN 140:22447
TI Statins may potentiate bisphosphonates anticancer properties: a new pharmacological approach?
AU Vincenzi, Bruno; Santini, Daniele; Avvisati, Giuseppe; Baldi, Alfonso; La Cesa, Annalisa; Tonini, Giuseppe
CS Oncology-Hematology Department, Bio-Medico University, Rome, 83 00155, Italy
SO Medical Hypotheses (2003), 61(1), 98-101

CODEN: MEHYDY; ISSN: 0306-9877
PB Elsevier Science Ltd.
DT Journal; **General Review**
LA English
AB A review. Both statins and bisphosphonates may inhibit cancer proliferation by two main different mechanisms: inducing apoptosis along cholesterol synthesis pathway and by antiangiogenic properties. Moreover, also an immunomediated mechanism could be involved in anticancer properties of these mols. The assocn. of these two drugs could represent an interesting pharmacol. approach in anticancer treatment. The available data offer the rationale for future in vitro studies aimed at evaluating proapoptotic and antiangiogenic action of this assocn. If the results of vitro studies should confirm the hypothesis that statins potentiate the action of bisphosphonates, further clin. investigations could be mandatory to evaluate the efficacy of this new pharmacol. approach in anticancer therapy.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 117 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:62276 HCAPLUS
DN 138:313726
TI Cyclooxygenase 2: a molecular target for cancer prevention and treatment
AU Subbaramaiah, Kotha; Dannenberg, Andrew J.
CS Dept of Medicine, Weill Medical College of Cornell University, New York, NY, 10021, USA
SO Trends in Pharmacological Sciences (2003), 24(2), 96-102
CODEN: TPHSDY; ISSN: 0165-6147
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review. Cyclooxygenase 2 (COX-2), an inducible prostaglandin G/H synthase, is overexpressed in several human cancers. Here, the potential utility of selective COX-2 inhibitors in the prevention and treatment of cancer is considered. The mechanisms by which COX-2 levels increase in cancers, key data that indicate a causal link between increased COX-2 activity and tumorigenesis, and possible mechanisms of action of COX-2 are discussed. In a proof-of-principle clin. trial, treatment with the selective COX-2 inhibitor celecoxib reduced the no. of colorectal polyps in patients with familial adenomatous polyposis. Selective COX-2 inhibitors appear to be sufficiently safe to permit large-scale clin. testing and numerous clin. trials are currently under way to det. whether selective inhibitors of COX-2 are effective in the prevention and treatment of cancer.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 118 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:204494 HCAPLUS
DN 139:285313
TI Potential Anticancer Effects of Statins: Fact or Fiction?
AU Kaushal, Varsha; Kohli, Manish; Mehta, Paulette; Mehta, Jawahar L.
CS Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, USA
SO Endothelium (2003), 10(1), 49-58
CODEN: ENDTE9; ISSN: 1062-3329
PB Taylor & Francis Ltd.

DT Journal; **General Review**
LA English
AB A review. Deregulation of any of the steps in cell growth, proliferation and apoptosis may result in its malignant transformation. Statins, along with their lipid-lowering potential, modify several processes in the cell cycle. These agents inhibit cell proliferation and arrest cell cycle progression by interrupting growth-promoting signals. Statins selectively induce proapoptotic protential in tumor cells and synergistically enhance proapoptotic potential of several cytotoxic agents. Statins alter angiogenic potential of cells by modulating apoptosis inhibitory effects of VEGF and decrease secretion of metalloproteases. Statins also alter adhesion and migration of tumor cells, thereby inhibiting tumor invasion and metastasis. Statins suppress rate of activation of multiple coagulation factors and thus prevent coagulation-mediated angiogenesis. Statins have been shown to have anti-tumor activity in exptl. models. Various anti-neoplastic properties of statins are probably a result of inhibition of posttranslational modifications of growth regulatory proteins. Mol. mechanisms of antiproliferative, proapoptotic and antiangiogenic effects of statins are reviewed in this chapter.
RE.CNT 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 119 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:675772 HCAPLUS
DN 137:195546
TI Treatment of HIV and viral diseases, vascular disease and cancer using a COX-2 inhibitor and cystine
IN Kindness, George; Schumm, Brooke, III; Guilford, Timothy F.
PA Probiochem, LLC, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002067853 A2		20020906	WO 2002-US2480	20020126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR

PRAI US 2000-PV238504 20001006
US 2000-PV238506 20001006
US 2000-PV243901 20001027
US 2000-PV243902 20001027
US 2000-PV245592 20001117
US 2001-PV264511 20010126
US 2001-PV264504 20010126
US 2001-PV307689 20010725
US 2001-912703 20010725
WO 2001-US31328 20011006
US 2001-997490 20011117

AB The invention discloses the combination of a selective COX-2 inhibitor and cystine for the treatment of anti-viral diseases, including HIV,

immuno-compromised individuals, AIDS and hepatitis C, atherosclerosis and related atherosclerosis vascular disease states, coronary ischemic syndrome, thrombosis, related vascular problems, cancer and to alleviate 5-hydroxy tryptamine- mediated mechanisms by at least relieving inflammatory symptoms, through regulation of cytokine activated responses, including migraine and migraine-like conditions, to ameliorate neurodegenerative diseases aggravated by inflammatory condition and carotidynia. An HMG-CoA reductase inhibitor may be added to enhance the combination. Magnesium sulfate or similar compd. is proposed to be added to enhance the treatment of neurodegenerative conditions.

L74 ANSWER 120 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:615422 HCAPLUS
DN 137:164123
TI Uroguanylin and cyclooxygenase-2 inhibitor combinations for inhibition of intestinal cancer
IN Masferrer, Jaime L.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002062369	A2	20020815	WO 2002-US3201	20020204
	WO 2002062369	A3	20030828		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1365753	A2	20031203	EP 2002-702137	20020204
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-265955P	P	20010202		
	WO 2002-US3201	W	20020204		

AB Disclosed is a method of retarding the development of polyps and prevention, inhibition and treatment of cancer in the intestine of a subject by administration of a compn. comprising a peptide with the active domain of uroguanylin or any agonist peptide or compd. binding to the guanylate cyclase receptor GC-C in the intestine in combination with a naturally occurring, derived from a naturally occurring, or a chem. synthesized cycloogenase-2 inhibitor, preferably a selective cyclooxygenase-2 inhibitor.

L74 ANSWER 121 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:869587 HCAPLUS
DN 137:346169
TI Combination and method of treatment of cancer utilizing a COX-2 inhibitor and an HMG-CoA inhibitor and cystine to enhance glutathione
IN Kindness, George; Schumm, Brooke; Guilford, F. Timothy

PA USA
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Pat. Appl. 2002 86,894.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169195	A1	20021114	US 2002-57511	20020126
US 2002086894	A1	20020704	US 2001-912703	20010725
US 6534540	B2	20030318		
WO 2002028270	A2	20020411	WO 2001-US31328	20011006
WO 2002028270	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2001-264511P	P	20010126
	US 2001-307689P	P	20010725
	US 2001-912703	A2	20010725
	WO 2001-US31328	W	20011006
	US 2000-238504P	P	20001006
	US 2000-238506P	P	20001006
	US 2000-243901P	P	20001027
	US 2000-243902P	P	20001027
	US 2000-245592P	P	20001117
	US 2001-263486P	P	20010123

AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer, esp. prostate cancer, and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer, esp. prostate cancer, and a method of treatment of cancer by that combination, esp. prostate cancer. Also contemplated is the addn. of lipoic acid and compds. to maintain adequate levels of selenium, Vitamin C and Vitamin E. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristic of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer. A patient with stage 4 metastatic prostate cancer was treated with Vioxx and Mevacor.

L74 ANSWER 122 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:717053 HCAPLUS
DN 137:226597
TI Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-a (HMG-CoA) reductase inhibitor
IN Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PA USA
SO U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of Appl. No. PCT/US01/31328.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002132781	A1	20020919	US 2001-997490	20011117
	US 2002086894	A1	20020704	US 2001-912703	20010725
	US 6534540	B2	20030318		
	WO 2002028270	A2	20020411	WO 2001-US31328	20011006
	WO 2002028270	A3	20020613		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2002067853	A2	20020126	WO 2002-US2480	20020126
	WO 2002067853	A3	20021031		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2002083124	A1	20021024	WO 2002-US2478	20020126
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2002094021	A1	20021128	WO 2002-US2477	20020126
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2000-238504P	P	20001006		
	US 2000-238506P	P	20001006		
	US 2000-243901P	P	20001027		
	US 2000-243902P	P	20001027		

US 2000-245592P P 20001103
US 2001-264511P P 20010126
US 2001-307689P P 20010725
US 2001-912703 P 20010725
WO 2001-US31328 W 20011006
US 2000-249592P P 20001117
US 2001-263486P P 20010123
US 2001-264504P P 20010126
US 2001-997490 A2 20011117
US 2002-352047P P 20020126

AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. Also contemplated is the addn. of lipoic acid and compds. to maintain adequate levels of selenium, vitamin C and vitamin E. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristics of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer.

L74 ANSWER 123 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:505414 HCAPLUS
DN 137:57551
TI Combination and method of treatment of cancer utilizing a COX-2 inhibitor and a 3-hydroxy-3-methylglutaryl-coenzyme-A (HMG-CoA) reductase inhibitor
IN Kindness, George; Schumm, Brooke; Guilford, F. Timothy
PA USA
SO U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002086894	A1	20020704	US 2001-912703	20010725
US 6534540	B2	20030318		
WO 2002028270	A2	20020411	WO 2001-US31328	20011006
WO 2002028270	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002013050	A5	20020415	AU 2002-13050	20011006
US 2002132781	A1	20020919	US 2001-997490	20011117
WO 2003022268	A1	20030320	WO 2001-US44050	20011117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
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CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002067853 A2 20020126 WO 2002-US2480 20020126
WO 2002067853 A3 20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002083124 A1 20021024 WO 2002-US2478 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002169195 A1 20021114 US 2002-57511 20020126
WO 2002094021 A1 20021128 WO 2002-US2477 20020126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003162829 A1 20030828 US 2003-390517 20030317
PRAI US 2000-245592P P 20001117
US 2001-263486P P 20010123
US 2001-264511P P 20010126
US 2000-238504P P 20001006
US 2000-238506P P 20001006
US 2000-243901P P 20001027
US 2000-243902P P 20001027
US 2000-249592P P 20001117
US 2001-264504P P 20010126
US 2001-307689P P 20010725
US 2001-912703 A2 20010725
WO 2001-US31328 W 20011006
US 2001-997490 A2 20011117
US 2002-352047P P 20020126
AB The inventors propose a combination of an HMG-CoA reductase inhibitor (also referred to as "HMG-CoA inhibitor(s)"), and COX-2 inhibitor for the

treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. The inventors propose a combination of an HMG-CoA reductase inhibitor, COX-2 inhibitor, and glutathione pathway enhancing and detoxifying compd., particularly cystine, for the treatment of cancer esp. prostate cancer and a method of treatment of cancer by that combination, esp. prostate cancer. Based on the clin. results of retardation, but not cure of cancer, the combination has the characteristic of sufficiently interfering with replication and apparently restoring the immune system capacity to manage cancer. An anticancer compn. comprises rofecoxib, lovastatin, and cystine.

L74 ANSWER 124 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:925262 HCAPLUS
DN 138:23665
TI Use of human anti-CTLA-4 antibodies for treatment of cancer
IN Hanson, Douglas Charles; Mueller, Eileen Elliott
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 76 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1262193	A1	20021204	EP 2002-253652	20020523
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2002371013	A2	20021226	JP 2002-142978	20020517
	AU 2002042421	A5	20021128	AU 2002-42421	20020521
	US 2003086930	A1	20030508	US 2002-153382	20020522
	CN 1404876	A	20030326	CN 2002-120349	20020523
PRAI	US 2001-293042P	P	20010523		

AB Anti-CTLA-4 antibodies, particularly human anti-CTLA-4 antibodies such as those having amino acid sequences of antibodies 3.1.1, 4.1.1, 4.8.1, 4.10.2, 4.13.1, 4.14.3, 6.1.1, 11.2.1, 11.6.1, 11.7.1, 12.3.1.1, and 12.9.1.1, are used in the treatment of certain cancers. The antibodies can be used in combination with chemotherapeutic agents, cancer vaccines, immunomodulatory agents, anti-angiogenesis agents, anti-vascular agents, signal transduction inhibitors, antiproliferative agents, or apoptosis inducers.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 125 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:596320 HCAPLUS
DN 138:180308
TI Celecoxib induces apoptosis by inhibiting 3-phosphoinositide-dependent protein kinase-1 activity in the human colon cancer HT-29 cell line
AU Arico, Sebastien; Pattingre, Sophie; Bauvy, Chantal; Gane, Pierre; Barbat, Alain; Codogno, Patrice; Ogier-Denis, Eric
CS INSERM U504 Glycobiologie et Signalisation Cellulaire, Villejuif, 94807, Fr.
SO Journal of Biological Chemistry (2002), 277(31), 27613-27621
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English

AB The cyclooxygenase-2 inhibitor celecoxib induced apoptosis in human colon cancer cell line HT-29 by inhibiting 3-phosphoinositide-dependent kinase 1 (PDK1) activity. This effect was correlated with inhibition of the phosphorylation of the PDK1 downstream substrate Akt/protein kinase B (PKB) on two regulatory sites, Thr308 and Ser473. However, expression of a constitutive active form of Akt/PKB (myristoylated PKB) had a low protective effect against celecoxib-induced cell death. In contrast, overexpression of a constitutive active mutant of PDK1 (PDK1A280V) was as potent as the pancaspase inhibitor benzyloxycarbonyl-Val-Ala-Asp-fluoromethyl ketone, to impair celecoxib-induced apoptosis. By contrast, cells expressing a kinase-defective mutant of PDK1 (PDK1K114G) remained sensitive to celecoxib. Furthermore, in vitro measurement revealed that celecoxib was a potential inhibitor of PDK1 activity, with an IC50 = 3.5 .mu.M. These data indicate that inhibition of PDK1 signaling is involved in the proapoptotic effect of celecoxib in HT-29 cells.
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 126 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:850915 HCAPLUS
DN 137:362164
TI COX inhibitor, suppression of polyposis, and chemoprevention
AU Oshima, Masanobu; Taketo, Makoto M.
CS Dep. Pharmacol., Kyoto Univ. Grad. Sch. Med., Kyoto, 606-8501, Japan
SO Nippon Yakurigaku Zasshi (2002), 120(5), 276-284
CODEN: NYKZAU; ISSN: 0015-5691
PB Nippon Yakuri Gakkai
DT Journal; General Review
LA Japanese
AB A review. Early expts. using carcinogen-induced rat intestinal tumor models demonstrated the inhibitory effects of non-steroidal anti-inflammatory drugs (NSAIDs) on intestinal tumorigenesis. Furthermore, epidemiol. studies and clin. trials for familial adenomatous polyposis (FAP) patients supported the possibility that NSAIDs can be used as chemopreventive agents. The major target mols. of NSAIDs are cyclooxygenases (COX), which catalyze the rate-limiting step of prostaglandin biosynthesis. Two isoenzymes of COX have been identified: COX-1 and COX-2. Whereas COX-1 is expressed constitutively in most tissues and responsible for tissue homeostasis, COX-2 is inducible and plays an important role in inflammation and tumorigenesis. A genetic study using compd. mutant mice of COX-2-/- and Apc.DELTA.716, a model for human familial adenomatous polyposis (FAP), directly demonstrated that induction of COX-2 is crit. for intestinal polyp formation. Numerous studies have also demonstrated that COX-2-selective inhibitors suppress intestinal polyp formation in Apc gene-mutant mice and xenografted cancer cell growths. In addn., stimulation of angiogenesis is one of the major effects by COX-2 expression that is induced in the polyp stromal cells. These data from animal model studies should be helpful in understanding the in vivo mechanism(s) of tumor suppression by NSAIDs or COX-2 inhibitors. The animal studies that reported the suppression of intestinal tumor growths by NSAIDs or COX-2 inhibitors were discussed.

L74 ANSWER 127 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:617820 HCAPLUS
DN 135:175361
TI Treatment or prevention of prostate cancer with a COX-2 selective inhibiting drug

IN Waldstreicher, Joanne; Morrison, Briggs W.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001060365	A1	20010823	WO 2001-US4655	20010213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1259237	A1	20021127	EP 2001-910637	20010213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003522790	T2	20030729	JP 2001-559462	20010213
US 2001041713	A1	20011115	US 2001-784878	20010216
PRAI US 2000-183204P	P	20000217		
WO 2001-US4655	W	20010213		

AB A COX-2 selective inhibiting drug is disclosed as useful in treating or preventing prostate cancer. The compd. is used alone or in combination with other drugs.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 128 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:169771 HCAPLUS
DN 134:361125
TI A reduction of tumor necrosis factor-.alpha. in paw exudate of lipopolysaccharide-treated rats by nimesulide
AU Azab, Abed N.; Kaplanski, Jacob
CS Department of Clinical Pharmacology, Ben-Gurion University of the Negev, Beer Sheva, 84105, Israel
SO Life Sciences (2001), 68(14), 1667-1675
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
AB This work studied the effect of the selective cyclooxygenase 2 inhibitor nimesulide on tumor necrosis factor-.alpha. (TNF-.alpha.) in the paw exudate of rats pretreated with lipopolysaccharide (LPS). Rats were injected (subplantar) with LPS (100 .mu.g/paw) in the right hind paw, which resulted in a prominent increase in paw exudate TNF-.alpha., which peaked 1 h postinjection. In rats pretreated with nimesulide (30 mg/kg, i.p.), the elevation of TNF-.alpha. in the paw exudate was reduced. These results further stress the multiple anti-inflammatory effects of nimesulide.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 129 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:688554 HCAPLUS
DN 135:369951
TI Activation of the PPAR pathway induces apoptosis and COX-2 inhibition in HT-29 human colon cancer cells
AU Yang, Wan-Lin; Frucht, Harold
CS Division of Oncologic Gastroenterology, Fox Chase Cancer Center, Philadelphia, PA, 19111, USA
SO Carcinogenesis (2001), 22(9), 1379-1383
CODEN: CRNGDP; ISSN: 0143-3334
PB Oxford University Press
DT Journal
LA English
AB The .gamma. isoform of the peroxisome proliferator-activated receptor (PPAR.gamma.) is a nuclear receptor that regulates adipocyte differentiation. Recently it has been shown to be expressed in human colonic mucosa and cancer, but its role in colon carcinogenesis and progression is still unclear. The authors demonstrate that activation of PPAR.gamma. by ciglitazone (cig), a selective PPAR.gamma. ligand, induces HT-29 human colon cancer cells to undergo apoptosis. Treatment with cig also down-regulates expression of cyclooxygenase-2 (COX-2) protein. Simultaneous exposure of cells to cig and 9-cis-retinoic acid (9-cis-RA), a ligand for retinoid X receptor, results in an increased apoptotic effect and increased inhibition of COX-2 expression, compared with cells treated with either cig or 9-cis-RA alone. As COX-2 is overexpressed in human colon cancer and has been implicated in augmenting invasiveness and tumorigenicity, the ability of PPAR.gamma. activation to decrease COX-2 expression and induce apoptosis suggests that the PPAR.gamma. pathway may be considered as a therapeutic target for colon cancer.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 130 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:340119 HCAPLUS
DN 135:313243
TI Indomethacin and telomerase activity in tumor growth retardation
AU Lonnroth, Christina; Andersson, Marianne; Lundholm, Kent
CS Surgical Metabolic Research Laboratory at Lundberg Laboratory for Cancer Research, Department of Surgery, Sahlgrenska University Hospital, Goteborg University, Goteborg, SE-413 45, Swed.
SO International Journal of Oncology (2001), 18(5), 929-937
CODEN: IJONES; ISSN: 1019-6439
PB International Journal of Oncology
DT Journal
LA English
AB This study showed that indomethacin retards MCG-101 tumor growth in mice by induction of apoptosis/necrosis and inhibits telomere elongation. The inhibition of telomerase activity by nonsteroidal anti-inflammatory drugs (NSAIDs) (indomethacin, mobic, sulindac sulfone, suramin) was, however, not a universal finding, since a mouse melanoma (K1735-M2) did not respond. By contrast, a human cell line of colon carcinoma origin (HT-29) responded by both retarded growth and telomerase activity despite a low intrinsic prodn. of prostaglandins, mainly PGE2. Therefore, it is not likely that indomethacin's inhibition of tumor growth and telomere elongation is directly related to cyclooxygenase-1/-2 activities in tumor cells. Also, NSAIDs (sulindac sulfone) at 25 .mu.M decreased growth and telomerase activity in MCG-101 cells, without any effects on PGE2 prodn.,

while ibuprofen reduced PGE2 prodn. but had no effect on growth or telomerase activity. The results demonstrate that cyclooxygenase inhibitors can retard tumor growth both in murine tumors and in human tumor cells by inhibition of telomerase activity, in addn. to previously recognized mechanisms such as induction of apoptosis, inhibition of cell proliferation, influence on the expression of growth factors around growing tumors and attenuation of neoangiogenesis.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 131 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:544445 HCAPLUS
DN 135:313306
TI Cyclooxygenase inhibitors retard murine mammary tumor progression by reducing tumor cell migration, invasiveness and angiogenesis
AU Rozic, Jerry G.; Chakraborty, Chandan; Lala, Peeyush K.
CS Department of Anatomy and Cell Biology, University of Western Ontario, London, ON, N6A 5C1, Can.
SO International Journal of Cancer (2001), 93(4), 497-506
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB This study examd. the role of endogenous prostaglandins in the proliferation/survival, the migratory and invasive behavior and angiogenic ability of a highly metastatic murine mammary tumor cell line, C3L5, originally derived from a C3H/HeJ spontaneous mammary tumor. This cell line was shown to express high levels of cyclooxygenase (COX) -2 mRNA and protein, as detected by Northern and Western blotting as well as immunostaining. PGE2 prodn. by C3L5 cells was primarily due to COX-2, since this was blocked similarly by the nonselective COX inhibitor indomethacin and the selective COX-2 inhibitor NS-398 but unaffected by the selective COX-1 inhibitor valeryl salicylate. C3L5 cell proliferation/survival in vitro was not influenced by prostaglandins, since their cellularity remained unaffected in the presence of PGE2 or NS-398 or the prostaglandin-receptor (EP1/EP2) antagonist AH6809; a marginal decline was caused only at high concns. of indomethacin, an effect which was not abrogated by addn. of exogenous PGE2. The migratory and invasive abilities of C3L5 cells, as quantitated by in vitro transwell migration/invasion assays, were inhibited by indomethacin or NS-398 or AH6809 in a concn.-dependent manner; the indomethacin- and NS-398-mediated inhibition was partially reversed by addn. of exogenous PGE2. An in vivo angiogenesis assay that used s.c. implants of growth factor-reduced matrigel inclusive of tumor cells showed inhibition of blood vessel formation in these implants in animals treated with indomethacin compared with animals receiving vehicle alone. These studies show that selective and nonselective COX-2 inhibitors retarded tumor progression in this COX-2-expressing murine mammary tumor model by inhibiting tumor cell migration, invasiveness and tumor-induced angiogenesis. The inhibitory effects were not entirely prostaglandin-dependent; some prostaglandin-independent effects were also noted.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 132 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:74130 HCAPLUS
DN 135:101746

TI Suppression of dolichol synthesis with isoprenoids and statins may potentiate the cancer-retardant efficacy of IGF-I down-regulation
AU McCarty, M. F.
CS Pantox Laboratories, San Diego, CA, 92109, USA
SO Medical Hypotheses (2001), 56(1), 12-16
CODEN: MEHYDY; ISSN: 0306-9877
PB Churchill Livingstone
DT Journal; **General Review**
LA English
AB A review, with 78 refs. Agents that inhibit the synthesis of mevalonate or of downstream isoprenoids block the G1-S transition and induce apoptosis in many cell lines; these agents include statins, phenylacetate, and a range of cyclic and acyclic isoprenoids. This cytostatic effect is mediated primarily by decreased availability of dolichol; this deficit impedes the glycosylation of nascent IGF-I receptors, preventing their transfer to the cell surface. In most tissues as well as transformed cell lines, IGF-I activity is crucial for transition to S phase, and also prevents apoptosis. Thus, down-regulation of serum levels of free IGF-I, as may be achieved by caloric restriction, low-fat vegan diets, and various estrogen agonists/antagonists, may represent a useful strategy for preventing and controlling cancer; however, a compensatory up-regulation of tissue expression of IGF-I receptors limits the efficacy of such an approach. Concurrent use of agents that inhibit dolichol synthesis can be expected to prevent an increase in plasma membrane IGF-I receptors, thus potentiating the cancer-retardant efficacy of IGF-I down-regulation. Since dolichol and IGF-I appear to be essential for angiogenesis, these measures may also prove useful for control of pathogenic neovascularization.
RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 133 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:783985 HCAPLUS
DN 134:305028
TI Meloxicam inhibits the growth of non-small-cell lung cancer
AU Tsubouchi, Yasunori; Mukai, Shigehiko; Kawahito, Yutaka; Yamada, Ryoji; Kohno, Masataka; Inoue, Ken-Ichiro; Sano, Hajime
CS First Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kyoto, 602-8566, Japan
SO Anticancer Research (2000), 20(5A), 2867-2872
CODEN: ANTRD4; ISSN: 0250-7005
PB International Institute of Anticancer Research
DT Journal
LA English
AB This work evaluated the effects of the preferential cyclooxygenase (COX)-2 inhibitor meloxicam on the growth of lung cancer cells. The reverse transcriptase-polymerase chain reaction and Western blot anal. showed that COX-2 but not COX-1 was expressed in human non-small-cell lung cancer (NSCLC) cell lines (A549 and PC14). In a human small-cell lung cancer cell line (H841), neither COX-1 nor COX-2 was detected. Meloxicam inhibited the growth of and PGE2 prodn. by both A549 and PC14, but not H841, cells. These findings suggest that COX-2 may play an important role in the pathogenesis and progression of NSCLC, and that meloxicam may be a useful therapeutic agent in the treatment of NSCLC.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 134 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:843004 HCAPLUS
DN 134:264071
TI Biochemistry of cyclooxygenase (COX)-2 inhibitors and molecular pathology of COX-2 in neoplasia
AU Fosslien, Egil
CS Department of Pathology, College of Medicine, University of Illinois at Chicago, Chicago, IL, 606 12, USA
SO Critical Reviews in Clinical Laboratory Sciences (2000), 37(5), 431-502
CODEN: CRCLBH; ISSN: 1040-8363
PB CRC Press LLC
DT Journal; General Review
LA English
AB A review with 333 refs. Several types of human tumors overexpress cyclooxygenase (COX)-2 but not COX-1, and gene knockout transfection expts. demonstrate a central role of COX-2 in exptl. tumorigenesis. COX-2 produces prostaglandins that inhibit apoptosis and stimulate angiogenesis and invasiveness. Selective COX-2 inhibitors reduce prostaglandin synthesis, restore apoptosis, and inhibit cancer cell proliferation. In animal studies they limit carcinogen-induced tumorigenesis. In contrast, aspirin-like nonselective NSAIDs such as sulindac and indomethacin inhibit not only the enzymic action of the highly inducible, proinflammatory COX-2 but the constitutively expressed, cytoprotective COX-1 as well. Consequently, nonselective NSAIDs can cause platelet dysfunction, gastrointestinal ulceration, and kidney damage. For that reason, selective inhibition of COX-2 to treat neoplastic proliferation is preferable to nonselective inhibition. Selective COX-2 inhibitors, such as meloxicam, celecoxib (SC-58635), and rofecoxib (MK-0966), are NSAIDs that have been modified chem. to preferentially inhibit COX-2 but not COX-1. For instance, meloxicam inhibits the growth of cultured colon cancer cells (HCA-7 and Moser-S) that express COX-2 but has no effect on HCT-116 tumor cells that do not express COX-2. NS-398 induces apoptosis in COX-2 expressing LNCaP prostate cancer cells and, surprisingly, in colon cancer S/KS cells that does not express COX-2. This effect may due to induction of apoptosis through uncoupling of oxidative phosphorylation and down-regulation of Bcl-2, as has been demonstrated for some nonselective NSAIDs, for instance, flurbiprofen. COX-2 mRNA and COX-2 protein is constitutively expressed in the kidney, brain, spinal cord, and ductus deferens, and in the uterus during implantation. In addn., COX-2 is constitutively and dominantly expressed in the pancreatic islet cells. These findings might somewhat limit the use of presently available selective COX-2 inhibitors in cancer prevention but will probably not deter their successful application for the treatment of human cancers.
RE.CNT 336 THERE ARE 336 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 135 OF 135 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:586059 HCAPLUS
DN 131:285766
TI Isoprenoid-mediated inhibition of mevalonate synthesis: potential application to cancer
AU Elson, Charles E.; Peffley, Dennis M.; Hentosh, Patricia; Mo, Huanbiao
CS Department of Nutritional Sciences, College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA
SO Proceedings of the Society for Experimental Biology and Medicine (1999), 221(4), 294-311
CODEN: PSEBAA; ISSN: 0037-9727

PB Blackwell Science, Inc.
DT Journal; **General Review**
LA English
AB A review with 315 refs. Pure and mixed isoprenoid end products of plant mevalonate metab. trigger actions that suppress 3-hydroxy-3-methylglutaryl CoA (HMG CoA) reductase activity. These actions modulate HMG CoA reductase mRNA translation and the proteolytic degrdn. of HMG CoA reductase. Such post-transcriptional events, we propose, are activated directly by acyclic isoprenoids and indirectly by cyclic isoprenoids. Isoprenoids, acting secondarily to the dominant transcriptional effector of sterologenesis, modestly lower cholesterol levels, if and only if, sterologenesis is not repressed by a satg. input of dietary cholesterol. An anomaly assocd. with tumor growth, a sterol feedback-resistant HMG CoA reductase activity, ensures a pool of sterologenic pathway intermediates. Such intermediates provide lipophilic anchors essential for membrane attachment and biol. activity of growth hormone receptors, nuclear lamins A and B, and oncogenic ras. Tumor HMG CoA reductase retains high sensitivity to the isoprenoid-mediated secondary regulation. Repression of mevalonate synthesis by plant-derived isoprenoids reduces ras and lamin B processing, arrests cells in G1, and initiates cellular apoptosis. This unique tumor cell-specific sensitivity allows isoprenoids to be used for tumor therapy, an application emulating that of the statins, but one free of adverse effects. When evaluated at levels provided by a typical diet, isoprenoids individually have no impact on cholesterol synthesis and tumor growth. Nonetheless, isoprenoid-mediated activities are additive, and sometimes synergistic. Therefore, the combined actions of the estd. 23,000 isoprenoid constituents of plant materials, acting in concert with other chemopreventive phytochems., may explain the lowered cancer risk assocd. with a diet rich in plant products. In contrast, that lowering of cancer risk does not correspond to supplemental intake of other dietary factors assocd. with fruits, vegetables, and cereal grains, namely fiber, .beta.-carotene, vitamin C, and vitamin E, and only weakly to supplemental folate.
RE.CNT 315 THERE ARE 315 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT